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(54) **Title:** NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION, ASSESSMENT, PREVENTION, AND THERAPY OF OVARIAN CANCER

(57) **Abstract:** The invention relates to newly discovered nucleic acid molecules and proteins associated with ovarian cancer. Compositions, kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers are provided.

NUCLEIC ACID MOLECULES AND PROTEINS FOR THE IDENTIFICATION, ASSESSMENT, PREVENTION, AND THERAPY OF OVARIAN CANCER

RELATED APPLICATIONS

The present application claims priority from U.S. provisional patent application serial no. 60/276,025, filed on March 14, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/325,149, filed on September 26, 2001. The present application also claims priority from U.S. provisional patent application serial no. 60/276,026, filed on March 14, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/324,967, filed September 26, 2001. The present application additionally claims priority from U.S. provisional patent application serial no. 60/311,732, filed August 10, 2001, which was abandoned on September 25, 2001, and from U.S. provisional patent application serial no. 60/325,102, filed September 26, 2001. The present application also claims priority from U.S. provisional patent application serial no. 60/323,580, filed September 19, 2001. All of the above applications are expressly incorporated by reference.

FIELD OF THE INVENTION

The field of the invention is ovarian cancer, including diagnosis, characterization, management, and therapy of ovarian cancer.

BACKGROUND OF THE INVENTION

Ovarian cancer is responsible for significant morbidity and mortality in populations around the world. Ovarian cancer is classified, on the basis of clinical and pathological features, in three groups, namely epithelial ovarian cancer (EOC; >90% of ovarian cancer in Western countries), germ cell tumors (*circa* 2-3% of ovarian cancer), and stromal ovarian cancer (*circa* 5% of ovarian cancer; Ozols *et al.*, 1997, *Cancer Principles and Practice of Oncology*, 5th ed., DeVita *et al.*, Eds. pp. 1502). Relative to EOC, germ cell tumors and stromal ovarian cancers are more easily detected and treated

at an early stage, translating into higher/better survival rates for patients afflicted with these two types of ovarian cancer.

There are numerous types of ovarian tumors, some of which are benign, and others of which are malignant. Treatment (including non-treatment) options and predictions of patient outcome depend on accurate classification of the ovarian cancer. Ovarian cancers are named according to the type of cells from which the cancer is derived and whether the ovarian cancer is benign or malignant. Recognized histological tumor types include, for example, serous, mucinous, endometrioid, and clear cell tumors. In addition, ovarian cancers are classified according to recognized grade and stage scales.

In grade I, the tumor tissue is well differentiated. In grade II, tumor tissue is moderately well differentiated. In grade III, the tumor tissue is poorly differentiated. This grade correlates with a less favorable prognosis than grades I and II. Stage I is generally confined within the capsule surrounding one (stage IA) or both (stage IB) ovaries, although in some stage I (*i.e.* stage IC) cancers, malignant cells may be detected in ascites, in peritoneal rinse fluid, or on the surface of the ovaries. Stage II involves extension or metastasis of the tumor from one or both ovaries to other pelvic structures. In stage IIA, the tumor extends or has metastasized to the uterus, the fallopian tubes, or both. Stage IIB involves extension of the tumor to the pelvis. Stage IIC is stage IIA or IIB in which malignant cells may be detected in ascites, in peritoneal rinse fluid, or on the surface of the ovaries. In stage III, the tumor comprises at least one malignant extension to the small bowel or the omentum, has formed extrapelvic peritoneal implants of microscopic (stage IIIA) or macroscopic (< 2 centimeter diameter, stage IIIB; > 2 centimeter diameter, stage IIIC) size, or has metastasized to a retroperitoneal or inguinal lymph node (an alternate indicator of stage IIIC). In stage IV, distant (*i.e.* non-peritoneal) metastases of the tumor can be detected.

The durations of the various stages of ovarian cancer are not presently known, but are believed to be at least about a year each (Richart *et al.*, 1969, *Am. J. Obstet. Gynecol.* 105:386). Prognosis declines with increasing stage designation. For example, 5-year survival rates for patients diagnosed with stage I, II, III, and IV ovarian cancer are 80%, 57%, 25%, and 8%, respectively.

Despite being the third most prevalent gynecological cancer, ovarian cancer is the leading cause of death among those afflicted with gynecological cancers. The disproportionate mortality of ovarian cancer is attributable to a substantial absence of symptoms among those afflicted with early-stage ovarian cancer and to difficulty diagnosing ovarian cancer at an early stage. Patients afflicted with ovarian cancer most often present with non-specific complaints, such as abnormal vaginal bleeding, gastrointestinal symptoms, urinary tract symptoms, lower abdominal pain, and generalized abdominal distension. These patients rarely present with paraneoplastic symptoms or with symptoms which clearly indicate their affliction. Presently, less than about 40% of patients afflicted with ovarian cancer present with stage I or stage II. Management of ovarian cancer would be significantly enhanced if the disease could be detected at an earlier stage, when treatments are much more generally efficacious.

Ovarian cancer may be diagnosed, in part, by collecting a routine medical history from a patient and by performing physical examination, x-ray examination, and chemical and hematological studies on the patient. Hematological tests which may be indicative of ovarian cancer in a patient include analyses of serum levels of proteins designated CA125 and DF3 and plasma levels of lysophosphatidic acid (LPA). Palpation of the ovaries and ultrasound techniques (particularly including endovaginal ultrasound and color Doppler flow ultrasound techniques) can aid detection of ovarian tumors and differentiation of ovarian cancer from benign ovarian cysts. However, a definitive diagnosis of ovarian cancer typically requires performing exploratory laparotomy of the patient.

Potential tests for the detection of ovarian cancer (*e.g.*, screening, reflex or monitoring) may be characterized by a number of factors. The "sensitivity" of an assay refers to the probability that the test will yield a positive result in an individual afflicted with ovarian cancer. The "specificity" of an assay refers to the probability that the test will yield a negative result in an individual not afflicted with ovarian cancer. The "positive predictive value" (PPV) of an assay is the ratio of true positive results (*i.e.* positive assay results for patients afflicted with ovarian cancer) to all positive results (*i.e.* positive assay results for patients afflicted with ovarian cancer + positive assay results for patients not afflicted with ovarian cancer). It has been estimated that in order for an assay to be an appropriate population-wide screening tool for ovarian cancer the

assay must have a PPV of at least about 10% (Rosenthal *et al.*, 1998, *Sem. Oncol.* 25:315-325). It would thus be desirable for a screening assay for detecting ovarian cancer in patients to have a high sensitivity and a high PPV. Monitoring and reflex tests would also require appropriate specifications.

Owing to the cost, limited sensitivity, and limited specificity of known methods of detecting ovarian cancer, screening is not presently performed for the general population. In addition, the need to perform laparotomy in order to diagnose ovarian cancer in patients who screen positive for indications of ovarian cancer limits the desirability of population-wide screening, such that a PPV even greater than 10% would be desirable.

Prior use of serum CA125 level as a diagnostic marker for ovarian cancer indicated that this method exhibited insufficient specificity for use as a general screening method. Use of a refined algorithm for interpreting CA125 levels in serial retrospective samples obtained from patients improved the specificity of the method without shifting detection of ovarian cancer to an earlier stage (Skakes, 1995, *Cancer* 76:2004). Screening for LPA to detect gynecological cancers including ovarian cancer exhibited a sensitivity of about 96% and a specificity of about 89%. However, CA125-based screening methods and LPA-based screening methods are hampered by the presence of CA125 and LPA, respectively, in the serum of patients afflicted with conditions other than ovarian cancer. For example, serum CA125 levels are known to be associated with menstruation, pregnancy, gastrointestinal and hepatic conditions such as colitis and cirrhosis, pericarditis, renal disease, and various non-ovarian malignancies. Serum LPA is known, for example, to be affected by the presence of non-ovarian gynecological malignancies. A screening method having a greater specificity for ovarian cancer than the current screening methods for CA125 and LPA could provide a population-wide screening for early stage ovarian cancer.

Presently greater than about 60% of ovarian cancers diagnosed in patients are stage III or stage IV cancers. Treatment at these stages is largely limited to cytoreductive surgery (when feasible) and chemotherapy, both of which aim to slow the spread and development of metastasized tumor. Substantially all late stage ovarian cancer patients currently undergo combination chemotherapy as primary treatment, usually a combination of a platinum compound and a taxane. Median survival for

responding patients is about one year. Combination chemotherapy involving agents such as doxorubicin, cyclophosphamide, cisplatin, hexamethylmelamine, paclitaxel, and methotrexate may improve survival rates in these groups, relative to single-agent therapies. Various recently-developed chemotherapeutic agents and treatment regimens have also demonstrated usefulness for treatment of advanced ovarian cancer. For example, use of the topoisomerase I inhibitor topectan, use of amifostine to minimize chemotherapeutic side effects, and use of intraperitoneal chemotherapy for patients having peritoneally implanted tumors have demonstrated at least limited utility. Presently, however, the 5-year survival rate for patients afflicted with stage III ovarian cancer is 25%, and the survival rate for patients afflicted with stage IV ovarian cancer is 8%.

In summary, the earlier ovarian cancer is detected, the aggressiveness of therapeutic intervention and the side effects associated with therapeutic intervention are minimized. More importantly, the earlier the cancer is detected, the survival rate and quality of life of ovarian cancer patients is enhanced. Thus, a pressing need exists for methods of detecting ovarian cancer as early as possible. There also exists a need for methods of detecting recurrence of ovarian cancer as well as methods for predicting and monitoring the efficacy of treatment. There further exists a need for new therapeutic methods for treating ovarian cancer. The present invention satisfies these needs.

SUMMARY OF THE INVENTION

The invention relates to cancer markers (hereinafter "markers" or "markers of the inventions"), which are listed in Tables 1-3. The invention provides nucleic acids and proteins that are encoded by or correspond to the markers (hereinafter "marker nucleic acids" and "marker proteins," respectively). The invention further provides antibodies, antibody derivatives and antibody fragments which bind specifically with such proteins and/or fragments of the proteins.

In one aspect, the invention relates to various diagnostic, monitoring, test and other methods related to ovarian cancer detection and therapy. In one embodiment, the invention provides a diagnostic method of assessing whether a patient has ovarian cancer or has higher than normal risk for developing ovarian cancer, comprising the steps of comparing the level of expression of a marker of the invention in a patient

sample and the normal level of expression of the marker in a control, *e.g.*, a sample from a patient without ovarian cancer. A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer or has higher than normal risk for developing ovarian cancer.

In a preferred embodiment of the diagnostic method, the marker is over-expressed by at least two-fold in at least about 20% of stage I ovarian cancer patients, stage II ovarian cancer patients, stage III ovarian cancer patients, stage IV ovarian cancer patients, grade I ovarian cancer patients, grade II ovarian cancer patients, grade III ovarian cancer patients, epithelial ovarian cancer patients, stromal ovarian cancer patients, germ cell ovarian cancer patients, malignant ovarian cancer patients, benign ovarian cancer patients, serous neoplasm ovarian cancer patients, mucinous neoplasm ovarian cancer patients, endometrioid neoplasm ovarian cancer patients and/or clear cell neoplasm ovarian cancer patients.

The diagnostic methods of the present invention are particularly useful for patients with an identified pelvic mass or symptoms associated with ovarian cancer. The methods of the present invention can also be of particular use with patients having an enhanced risk of developing ovarian cancer (*e.g.*, patients having a familial history of ovarian cancer, patients identified as having a mutant oncogene, and patients at least about 50 years of age).

In a preferred diagnostic method of assessing whether a patient is afflicted with ovarian cancer (*e.g.*, new detection ("screening"), detection of recurrence, reflex testing), the method comprises comparing:

a) the level of expression of a marker of the invention in a patient sample, and

b) the normal level of expression of the marker in a control non-ovarian cancer sample.

A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer.

The invention also provides diagnostic methods for assessing the efficacy of a therapy for inhibiting ovarian cancer in a patient. Such methods comprise comparing:

a) expression of a marker of the invention in a first sample obtained from the patient prior to providing at least a portion of the therapy to the patient, and

b) expression of the marker in a second sample obtained from the patient following provision of the portion of the therapy.

A significantly lower level of expression of the marker in the second sample relative to that in the first sample is an indication that the therapy is efficacious for inhibiting ovarian cancer in the patient.

It will be appreciated that in these methods the "therapy" may be any therapy for treating ovarian cancer including, but not limited to, chemotherapy, radiation therapy, surgical removal of tumor tissue, gene therapy and biologic therapy such as the administering of antibodies and chemokines. Thus, the methods of the invention may be used to evaluate a patient before, during and after therapy, for example, to evaluate the reduction in tumor burden.

In a preferred embodiment, the diagnostic methods of the present invention are directed to therapy using a chemical or biologic agent. These methods comprise comparing:

a) expression of a marker of the invention in a first sample obtained from the patient and maintained in the presence of the chemical or biologic agent, and

b) expression of the marker in a second sample obtained from the patient and maintained in the absence of the agent.

A significantly lower level of expression of the marker in the first sample relative to that in the second sample is an indication that the agent is efficacious for inhibiting ovarian cancer in the patient. In one embodiment, the first and second samples can be portions of a single sample obtained from the patient or portions of pooled samples obtained from the patient.

The invention additionally provides a monitoring method for assessing the progression of ovarian cancer in a patient, the method comprising:

a) detecting in a patient sample at a first time point, the expression of a marker of the invention;

b) repeating step a) at a subsequent time point in time; and

c) comparing the level of expression detected in steps a) and b), and therefrom monitoring the progression of ovarian cancer in the patient.

A significantly higher level of expression of the marker in the sample at the subsequent time point from that of the sample at the first time point is an indication that the ovarian cancer has progressed, whereas a significantly lower level of expression is an indication that the ovarian cancer has regressed.

The invention further provides a diagnostic method for determining whether ovarian cancer has metastasized or is likely to metastasize in the future, the method comprising comparing:

a) the level of expression of a marker of the invention in a patient sample, and

b) the normal level (or non-metastatic level) of expression of the marker in a control sample.

A significantly higher level of expression in the patient sample as compared to the normal level (or non-metastatic level) is an indication that the ovarian cancer has metastasized or is likely to metastasize in the future.

The invention moreover provides a test method for selecting a composition for inhibiting ovarian cancer in a patient. This method comprises the steps of:

a) obtaining a sample comprising cancer cells from the patient;

b) separately maintaining aliquots of the sample in the presence of a plurality of test compositions;

c) comparing expression of a marker of the invention in each of the aliquots; and

d) selecting one of the test compositions which significantly reduces the level of expression of the marker in the aliquot containing that test

composition, relative to the levels of expression of the marker in the presence of the other test compositions.

The invention additionally provides a test method of assessing the ovarian carcinogenic potential of a compound. This method comprises the steps of:

a) maintaining separate aliquots of ovarian cells in the presence and absence of the compound; and

b) comparing expression of a marker of the invention in each of the aliquots.

A significantly higher level of expression of the marker in the aliquot maintained in the presence of the compound, relative to that of the aliquot maintained in the absence of the compound, is an indication that the compound possesses ovarian carcinogenic potential.

In addition, the invention further provides a method of inhibiting ovarian cancer in a patient. This method comprises the steps of:

a) obtaining a sample comprising cancer cells from the patient;

b) separately maintaining aliquots of the sample in the presence of a plurality of compositions;

c) comparing expression of a marker of the invention in each of the aliquots; and

d) administering to the patient at least one of the compositions which significantly lowers the level of expression of the marker in the aliquot containing that composition, relative to the levels of expression of the marker in the presence of the other compositions.

In the aforementioned methods, the samples or patient samples comprise cells obtained from the patient. The cells may be found in an ovarian tissue sample collected, for example, by an ovarian tissue biopsy or histology section. In one embodiment, the patient sample is an ovary-associated body fluid. Such fluids include, for example, blood fluids, lymph, ascites fluids, gynecological fluids, cystic fluids, urine, and fluids collected by peritoneal rinsing. In another embodiment, the sample comprises cells obtained from the patient. In this embodiment, the cells may be found in a fluid selected from the group consisting of a fluid collected by peritoneal rinsing, a fluid collected by uterine rinsing, a uterine fluid, a uterine exudate, a pleural fluid, and an ovarian exudate. In a further embodiment, the patient sample is *in vivo*.

According to the invention, the level of expression of a marker of the invention in a sample can be assessed, for example, by detecting the presence in the sample of:

- the corresponding marker protein or a fragment of the protein (*e.g.* by using a reagent, such as an antibody, an antibody derivative, an antibody fragment or single-chain antibody, which binds specifically with the protein or protein fragment).
- the corresponding marker nucleic acid or a fragment of the nucleic acid (*e.g.* by contacting transcribed polynucleotides obtained from the sample with a substrate having affixed thereto one or more nucleic acids having the entire or a segment of the sequence or a complement thereof)
- a metabolite which is produced directly (*i.e.*, catalyzed) or indirectly by the corresponding marker protein.

According to the invention, any of the aforementioned methods may be performed using a plurality (*e.g.* 2, 3, 5, or 10 or more) of ovarian cancer markers, including ovarian cancer markers known in the art. In such methods, the level of expression in the sample of each of a plurality of markers, at least one of which is a marker of the invention, is compared with the normal level of expression of each of the plurality of markers in samples of the same type obtained from control humans not afflicted with ovarian cancer. A significantly altered (*i.e.*, increased or decreased as specified in the above-described methods using a single marker) level of expression in the sample of one or more markers of the invention, or some combination thereof, relative to that marker's corresponding normal levels, is an indication that the patient is afflicted with ovarian cancer. For all of the aforementioned methods, the marker(s) are preferably selected such that the positive predictive value of the method is at least about 10%.

In a further aspect, the invention provides an antibody, an antibody derivative, or an antibody fragment, which binds specifically with a marker protein or a fragment of the protein. The invention also provides methods for making such antibody, antibody derivative, and antibody fragment. Such methods may comprise immunizing a mammal with a protein or peptide comprising the entirety, or a segment of 10 amino acids or more, of a marker protein, wherein the protein or peptide may be obtained from

a cell or by chemical synthesis. The methods of the invention also encompass producing monoclonal and single-chain antibodies, which would further comprise isolating splenocytes from the immunized mammal, fusing the isolated splenocytes with an immortalized cell line to form hybridomas, and screening individual hybridomas for those that produce an antibody that binds specifically with a marker protein or a fragment of the protein.

In another aspect, the invention relates to various diagnostic and test kits. In one embodiment, the invention provides a kit for assessing whether a patient is afflicted with ovarian cancer. The kit comprises a reagent for assessing expression of a marker of the invention. In another embodiment, the invention provides a kit for assessing the suitability of a chemical or biologic agent for inhibiting an ovarian cancer in a patient. Such kit comprises a reagent for assessing expression of a marker of the invention, and may also comprise one or more of such agents. In a further embodiment, the invention provides kits for assessing the presence of ovarian cancer cells or treating ovarian cancers. Such kits comprise an antibody, an antibody derivative, or an antibody fragment, which binds specifically with a marker protein, or a fragment of the protein. Such kits may also comprise a plurality of antibodies, antibody derivatives, or antibody fragments wherein the plurality of such antibody agents binds specifically with a marker protein, or a fragment of the protein.

In an additional embodiment, the invention also provides a kit for assessing the presence of ovarian cancer cells, wherein the kit comprises a nucleic acid probe that binds specifically with a marker nucleic acid or a fragment of the nucleic acid. The kit may also comprise a plurality of probes, wherein each of the probes binds specifically with a marker nucleic acid, or a fragment of the nucleic acid.

In a further aspect, the invention relates to methods for treating a patient afflicted with ovarian cancer or at risk of developing ovarian cancer. Such methods may comprise reducing the expression and/or interfering with the biological function of a marker of the invention. In one embodiment, the method comprises providing to the patient an antisense oligonucleotide or polynucleotide complementary to a marker nucleic acid, or a segment thereof. For example, an antisense polynucleotide may be provided to the patient through the delivery of a vector that expresses an antisense polynucleotide of a marker nucleic acid or a fragment thereof. In another embodiment,

the method comprises providing to the patient an antibody, an antibody derivative, or antibody fragment, which binds specifically with a marker protein or a fragment of the protein. In a preferred embodiment, the antibody, antibody derivative or antibody fragment binds specifically with a protein having the sequence of any of the markers listed in Table 1, or a fragment of such a protein.

It will be appreciated that the methods and kits of the present invention may also include known cancer markers including known ovarian cancer markers. It will further be appreciated that the methods and kits may be used to identify cancers other than ovarian cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 depicts a graph which represents the results of the TaqMan® expression study.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to newly discovered markers, identified in Tables 1-3, that are associated with the cancerous state of ovarian cells. It has been discovered that the higher than normal level of expression of any of these markers or combination of these markers correlates with the presence of ovarian cancer in a patient. Methods are provided for detecting the presence of ovarian cancer in a sample, the absence of ovarian cancer in a sample, the stage of an ovarian cancer, and with other characteristics of ovarian cancer that are relevant to prevention, diagnosis, characterization, and therapy of ovarian cancer in a patient. Methods of treating ovarian cancer are also provided.

Tables 1-3 list the markers of the present invention. In the Tables the markers are identified with a name ("Marker"), the name the gene is commonly known by, if applicable ("Gene Name"), the Sequence Listing identifier of the cDNA sequence of a nucleotide transcript encoded by or corresponding to the marker ("SEQ ID NO (nts)"), the Sequence Listing identifier of the amino acid sequence of a protein encoded by the nucleotide transcript ("SEQ ID NO (AAs)"), and the location of the protein coding sequence within the cDNA sequence ("CDS").

Table 1 lists all of the markers of the invention, which are over-expressed in ovarian cancer cells compared to normal (*i.e.*, non-cancerous) ovarian cells and comprises markers listed in Tables 2 and 3. Table 2 lists newly-identified nucleotide

and amino acid sequences useful as ovarian cancer markers. Table 3 lists newly-identified nucleotide sequences useful as ovarian cancer markers.

In addition to their use in ovarian cancer, it has been found that the markers of the present invention may be used in the diagnosis, characterization, management, and therapy of additional diseases. For example, OV65 (SEQ ID NOS: 305 and 306), M593 (SEQ ID NOS: 307 and 308) and M594 (SEQ ID NOS: 309 and 310), are spondin molecules, and have one or more of the following activities: (1) neural cell adhesion and (2) neurite extension and can thus be used in, for example, the diagnosis and treatment of brain and CNS related disorders. Such brain and CNS related disorders include, but are not limited to, bacterial and viral meningitis, Alzheimers Disease, cerebral toxoplasmosis, Parkinson's disease, multiple sclerosis, brain cancers (*e.g.*, metastatic carcinoma of the brain, glioblastoma, lymphoma, astrocytoma, acoustic neuroma), hydrocephalus, and encephalitis. In another example, OV65, M593 and M594 polypeptides, nucleic acids, and modulators thereof can be used to treat disorders of the brain, such as cerebral edema, hydrocephalus, brain herniations, iatrogenic disease (due to, *e.g.*, infection, toxins, or drugs), inflammations (*e.g.*, bacterial and viral meningitis, encephalitis, and cerebral toxoplasmosis), cerebrovascular diseases (*e.g.*, hypoxia, ischemia, infarction, intracranial hemorrhage, vascular malformations, and hypertensive encephalopathy), and tumors (*e.g.*, neuroglial tumors, neuronal tumors, tumors of pineal cells, meningeal tumors, primary and secondary lymphomas, intracranial tumors, and medulloblastoma), and to treat injury or trauma to the brain.

OV25 (SEQ ID NOS: 360 and 361), an HE4 protein, has one or more of the following activities: (1) sperm maturation and (2) inhibition of extracellular proteases and can thus be used in, for example, the treatment and diagnosis of diseases and disorders relating to spermatogenesis. For example, OV25 polypeptides, nucleic acids, and modulators thereof can be used to treat testicular disorders, such as unilateral testicular enlargement (*e.g.*, nontuberculous, granulomatous orchitis); inflammatory diseases resulting in testicular dysfunction (*e.g.*, gonorrhea and mumps); cryptorchidism; sperm cell disorders (*e.g.*, immotile cilia syndrome and germinal cell aplasia); acquired testicular defects (*e.g.*, viral orchitis); and tumors (*e.g.*, germ cell tumors, interstitial cell tumors, androblastoma, testicular lymphoma and adenomatoid tumors).

OV52 (SEQ ID NOS: 190 and 191), a Pump-1 proteinase, has been found to have one or more of the following activities: (1) breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and remodeling, as well as in (2) disease processes, such as arthritis, and metastasis. Hence, OV52 nucleic acids, proteins, and modulators thereof can be used to modulate disorders associated with adhesion and migration of cells, *e.g.*, platelet aggregation disorders (*e.g.*, Glanzmann's thromboasthemia, which is a bleeding disorder characterized by failure of platelet aggregation in response to cell stimuli), inflammatory disorders (*e.g.*, leukocyte adhesion deficiency, which is a disorder associated with impaired migration of neutrophils to sites of extravascular inflammation), connective tissue disorders, arthritis, disorders associated with abnormal tissue migration during embryo development, and tumor metastasis.

M604 (SEQ ID NOS: 48 and 49), OV10 (SEQ ID NOS: 50 and 51), and M360 (SEQ ID NOS: 52 and 53), are Claudin molecules which have one or more of the following activities: (1) it elicits fluid accumulation in the intestinal tract by altering the membrane permeability of intestinal epithelial cells and (2) thus acts as the causative agent of diarrhea. The polypeptides, nucleic acids, and modulators thereof can be used to treat colonic disorders, such as congenital anomalies (*e.g.*, megacolon and imperforate anus), idiopathic disorders (*e.g.*, diverticular disease and mèlanosis coli), vascular lesions (*e.g.*, ischemic colistis, hemorrhoids, angiodysplasia), inflammatory diseases (*e.g.*, colitis (*e.g.*, idiopathic ulcerative colitis, pseudomembranous colitis), and lymphopathia venereum), Crohn's disease, and tumors (*e.g.*, hyperplastic polyps, adenomatous polyps, bronchogenic cancer, colonic carcinoma, squamous cell carcinoma, adenoacanthomas, sarcomas, lymphomas, argentaffinomas, carcinoids, and melanocarcinomas).

OV48 (SEQ ID NOS: 226 and 227), OV49 (SEQ ID NOS: 228 and 229) and OV50 (SEQ ID NOS: 230 and 231), markers for an osteopontin protein, have one or more of the following activities: (1) they act as a vessel extracellular matrix protein involved in calcification and (2) atherosclerosis. Hence, OV48, OV49 and OV50 nucleic acids, proteins, and modulators thereof can be used to treat heart disorders, *e.g.*, ischemic heart disease, atherosclerosis, hypertension, angina pectoris, Hypertrophic Cardiomyopathy, and congenital heart disease. They can also be used to treat

cardiovascular disorders, such as ischemic heart disease (*e.g.*, angina pectoris, myocardial infarction, and chronic ischemic heart disease), hypertensive heart disease, pulmonary heart disease, valvular heart disease (*e.g.*, rheumatic fever and rheumatic heart disease, endocarditis, mitral valve prolapse, and aortic valve stenosis), congenital heart disease (*e.g.*, valvular and vascular obstructive lesions, atrial or ventricular septal defect, and patent ductus arteriosus), or myocardial disease (*e.g.*, myocarditis, congestive cardiomyopathy, and hypertrophic cariomyopathy).

OV37 (SEQ ID NOS: 176 and 177), a lipocalin marker, is known to be a component of the neutrophil gelatinase complex. OV37 nucleic acids, proteins, and modulators thereof can be used to modulate the proliferation, differentiation, and/or function of leukocytes. Thus, OV37 nucleic acids, proteins, and modulators thereof can be used to treat bone marrow, blood, and hematopoietic associated diseases and disorders, *e.g.*, acute myeloid leukemia, hemophilia, leukemia, anemia (*e.g.*, sickle cell anemia), and thalassemia. OV37 polypeptides, nucleic acids, and modulators thereof can be used to treat leukocytic disorders, such as leukopenias (*e.g.*, neutropenia, monocytopenia, lymphopenia, and granulocytopenia), leukocytosis (*e.g.*, granulocytosis, lymphocytosis, eosinophilia, monocytosis, acute and chronic lymphadenitis), malignant lymphomas (*e.g.*, Non-Hodgkin's lymphomas, Hodgkin's lymphomas, leukemias, agnogenic myeloid metaplasia, multiple myeloma, plasmacytoma, Waldenstrom's macroglobulinemia, heavy-chain disease, monoclonal gammopathy, histiocytoses, eosinophilic granuloma, and angioimmunoblastic lymphadenopathy).

OV2 (SEQ ID NOS: 285 and 286), is known to be a protease inhibitor, which is associated with emphysema and liver disease. Hence OV2 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat pulmonary (lung) disorders, such as atelectasis, cystic fibrosis, rheumatoid lung disease, pulmonary congestion or edema, chronic obstructive airway disease (*e.g.*, emphysema, chronic bronchitis, bronchial asthma, and bronchiectasis), diffuse interstitial diseases (*e.g.*, sarcoidosis, pneumoconiosis, hypersensitivity pneumonitis, bronchiolitis, Goodpasture's syndrome, idiopathic pulmonary fibrosis, idiopathic pulmonary hemosiderosis, pulmonary alveolar proteinosis, desquamative interstitial pneumonitis, chronic interstitial pneumonia, fibrosing alveolitis, hamman-rich syndrome, pulmonary eosinophilia, diffuse interstitial fibrosis, Wegener's granulomatosis, lymphomatoid

granulomatosis, and lipid pneumonia), or tumors (*e.g.*, bronchogenic carcinoma, bronchiolovlveolar carcinoma, bronchial carcinoid, hamartoma, and mesenchymal tumors). In another example, OV2 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat hepatic (liver) disorders, such as jaundice, hepatic failure, hereditary hyperbiliruinemias (*e.g.*, Gilbert's syndrome, Crigler-Naijar syndromes and Dubin-Johnson and Rotor's syndromes), hepatic circulatory disorders (*e.g.*, hepatic vein thrombosis and portal vein obstruction and thrombosis), hepatitis (*e.g.*, chronic active hepatitis, acute viral hepatitis, and toxic and drug-induced hepatitis), cirrhosis (*e.g.*, alcoholic cirrhosis, biliary cirrhosis, and hemochromatosis), or malignant tumors (*e.g.*, primary carcinoma, hepatoma, hepatoblastoma, liver cysts, and angiosarcoma).

OV32 (SEQ ID NOS: 166 and 167) and OV33 (SEQ ID NOS: 168 and 169), kallikrein markers, are useful in detection of primary mammary carcinomas, as well as primary ovarian cancers. Hence, OV32 and OV33 polypeptides, nucleic acids, and modulators thereof can be used to diagnose and treat ovarian disorders, such as ovarian endometriosis, non-neoplastic cysts (*e.g.*, follicular and luteal cysts and polycystic ovaries) and tumors (*e.g.*, carcinomas, tumors of surface epithelium, germ cell tumors, ovarian fibroma, sex cord-stromal tumors, and ovarian cancers (*e.g.*, metastatic carcinomas, and ovarian teratoma)).

OV68 (SEQ ID NOS: 192 and 193), OV69 (SEQ ID NOS: 194 and 195), OV70 (SEQ ID NOS: 196 and 197), OV71 (SEQ ID NOS: 198 and 199), OV72 (SEQ ID NOS: 200 and 201), OV41 (SEQ ID NOS: 202 and 203), OV42 (SEQ ID NOS: 204 and 205), OV43 (SEQ ID NOS: 206 and 205), OV44 (SEQ ID NOS: 207 and 208) and OV83 (SEQ ID NOS: 209 and 210), are all mesothelin markers, and have been found to play a role in cellular adhesion. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate disorders associated with adhesion and migration of cells, *e.g.*, platelet aggregation disorders (*e.g.*, Glanzmann's thromboasthemia, which is a bleeding disorder characterized by failure of platelet aggregation in response to cell stimuli), inflammatory disorders (*e.g.*, leukocyte adhesion deficiency, which is a disorder associated with impaired migration of neutrophils to sites of extravascular inflammation), disorders associated with abnormal tissue migration during embryo development, and tumor metastasis.

OV17 (SEQ ID NOS: 110 and 111), OV18 (SEQ ID NOS: 112 and 111), OV19 (SEQ ID NOS: 113 and 111), OV20 (SEQ ID NOS: 114 and 111), OV21 (SEQ ID NOS: 115 and 111) and OV22 (SEQ ID NOS: 116 and 117) are folate receptors, which are known to be markers of ovarian cancer. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate ovarian disorders (*e.g.*, ovarian cyst, ovarian fibroma, ovarian endometriosis, ovarian teratoma). Although these markers have been previously associated with ovarian cancer, the expression of such markers has not yet been identified in combination with the expression of other markers including those of the present invention. Such combination of markers will provide improved methods of diagnosing, characterizing, managing and treating ovarian cancer.

OV66 (SEQ ID NOS: 54 and 55), OV7 (SEQ ID NOS: 56 and 57), OV8 (SEQ ID NOS: 58 and 59) and OV81 (SEQ ID NOS: 60 and 61) are ceruloplasmin markers, known to encode a plasma metalloprotein that binds copper in the plasma. The nucleic acids, proteins, and modulators thereof can be used to diagnose, treat and modulate disorders in blood haemostasis and diseases caused by such an imbalance *e.g.*, (1) cardiovascular diseases or disorders, such as ischemic heart disease (*e.g.*, angina pectoris, myocardial infarction, and chronic ischemic heart disease), hypertensive heart disease, pulmonary heart disease, valvular heart disease (*e.g.*, rheumatic fever and rheumatic heart disease, endocarditis, mitral valve prolapse, and aortic valve stenosis), congenital heart disease (*e.g.*, valvular and vascular obstructive lesions, atrial or ventricular septal defect, and patent ductus arteriosus), or myocardial disease (*e.g.*, myocarditis, congestive cardiomyopathy, and hypertrophic cariomyopathy); (2) neuronal diseases such as Alzheimers Disease, cerebral toxoplasmosis, Parkinson's disease, multiple sclerosis, brain cancers (*e.g.*, metastatic carcinoma of the brain, glioblastoma, lymphoma, astrocytoma, acoustic neuroma), hydrocephalus, and encephalitis; and (3) Wilson's Disease.

TABLE 1

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
OV1	ABCB1: ATP-binding cassette, sub-family B (MDR/TAP), member 1	1	2	425..4264
M430	ADPRT: ADP-ribosyltransferase	3	4	160..3204
M571	ANXA2: annexin A2, variant 1	5	6	134..1153
M572	ANXA2: annexin A2, variant 2	7	8	50..1069
M573	ANXA4: annexin A4	9	10	74..1039
OV3	AQP5: aquaporin 5	11	12	519..1316
M352	ARHGAP8: Rho GTPase activating protein 8, variant 1	13	14	142..1536
M353	ARHGAP8: Rho GTPase activating protein 8, variant 2	15	16	1..2043
M354	ARHGAP8: Rho GTPase activating protein 8, variant 3	17	18	1..2256
M608	ARHGAP8: Rho GTPase activating protein 8, variant 4	17	19	1..2157
M355	ARHGAP8: Rho GTPase activating protein 8, variant 5	20	21	<1..1314
M356	ARHGAP8: Rho GTPase activating protein 8, variant 6	22	23	1..1902
M357	ARHGAP8: Rho GTPase activating protein 8, variant 7	24	25	<1..1281
M358	ARHGAP8: Rho GTPase activating protein 8, variant 8	26	27	1..1386
M359	ARHGAP8: Rho GTPase activating protein 8, variant 9	28	29	<1..1059
OV5	BICD1: Bicaudal D homolog 1 (Drosophila)	30	31	82..3009
M431	BTG2: BTG family, member 2	32	33	72..548
M432	CADPS: Ca2+-dependent activator protein for secretion	34	35	240..4412
M609	CDH1: cadherin 1, type 1, E-cadherin (epithelial)	36	37	125..2773
M433	CDH6: cadherin 6, type 2, K-cadherin	38	39	327..2699
M434	CDKN2A: cyclin-dependent kinase inhibitor 2A	40	41	41..511
OV9	CGN: cingulin	42	43	152..3763
OV6	CHI3L1: cartilage glycoprotein-39	44	45	127..1278
M435	CKMT1: creatine kinase, mitochondrial 1 (ubiquitous)	46	47	164..1417
M604	CLDN10: claudin 10	48	49	36..772
OV10	CLDN16: claudin 16	50	51	69..986
M360	CLDN4: claudin 4	52	53	183..812
OV66	CP: ceruloplasmin (ferroxidase), variant 1	54	55	1..3210
OV7	CP: ceruloplasmin (ferroxidase), variant 2	56	57	<1..2561
OV8	CP: ceruloplasmin (ferroxidase), variant 3	58	59	1..3198
OV81	CP: ceruloplasmin (ferroxidase), variant 4	60	61	76..3348
M103	CRABP2: cellular retinoic acid-binding protein 2	62	63	138..554

OV40	DD96: Epithelial protein up-regulated in carcinoma, membrane associated protein 17	64	65	202..546
OV4	DEC2: basic helix-loop-helix protein	66	67	135..1583
M575	dehydrogenase	68	69	339..1364
M436	DLX5: distal-less homeo box 5	70	71	204..1073
OV12	EAB1: Eab1 protein	72	73	<1..1305
OV13	ESX protein	74	75	96..1211
OV67	EVI-1: Evi-1 protein, variant 1	76	77	250..2406
OV14	EVI-1: Evi-1 protein, variant 2	78	79	250..3405
OV15	EVI-1: Evi-1 protein, variant 3	80	81	250..2433
OV16	EVI-1: Evi-1 protein, variant 4	82	83	250..3378
M437	FLJ10546: hypothetical protein FLJ10546	84	85	28..1815
OV28	FLJ12799: hypothetical protein FLJ12799	86	87	39..797
M576	FLJ13710: hypothetical protein FLJ13710	88	89	96..1712
M438	FLJ13782: hypothetical protein FLJ13782	90	91	13..1890
OV29	FLJ20150: hypothetical protein FLJ20150	92	93	78..983
M439	FLJ20327: hypothetical protein FLJ20327	94	95	306..2186
M440	FLJ20758: hypothetical protein FLJ20758, variant 1	96	97	<2..1270
M441	FLJ20758: hypothetical protein FLJ20758, variant 2	98	99	<2..2095
M442	FLJ20758: hypothetical protein FLJ20758, variant 3	100	101	465..1307
M443	FLJ22252: likely ortholog of mouse SRY-box containing gene 17	102	103	205..1449
M444	FLJ22316: hypothetical protein FLJ22316	104	105	508..1206
M400	FLJ22418: hypothetical protein FLJ22418	106	107	71..919
M445	FLJ23499: hypothetical protein FLJ23499	108	109	21..473
OV17	FOLR1: folate receptor 1 (alpha), variant 1	110	111	139..912
OV18	FOLR1: folate receptor 1 (alpha), variant 2	112	111	211..984
OV19	FOLR1: folate receptor 1 (alpha), variant 3	113	111	46..819
OV20	FOLR1: folate receptor 1 (alpha), variant 4	114	111	437..1210
OV21	FOLR1: folate receptor 1 (alpha), variant 5	115	111	11..784
OV22	FOLR3: folate receptor 3 (gamma)	116	117	57..788
OV23	GPR39: G protein-coupled receptor 39	118	119	1..1362
M446	GPRC5B: G protein-coupled receptor, family C, group 5, member B	120	121	109..1320
OV24	G-protein coupled receptor	122	123	274..1236
M447	GRB7: growth factor receptor-bound protein 7	124	125	220..1818
OV11	HAIK1: type I intermediate filament cytokeratin	126	127	61..1329
M448	HOXB7: homeo box B7	128	129	100..753
M138	HSECP1: secretory protein, variant 1	130	131	27..863
M449	HSECP1: secretory protein, variant 2	132	133	136..768
M450	HSECP1: secretory protein, variant 3	134	135	202..933
M451	HSNFRK: HSNFRK protein	136	137	642..2939
OV26	hypothetical protein (1)	138	139	<1..1140
OV27	hypothetical protein (2)	140	141	242..1483
OV31	IFI30: interferon, gamma-inducible protein 30	142	143	41..952
OV58	IGF2: somatomedin A	144	145	553..1095

M452	IMP-2: IGF-II mRNA-binding protein 2	146	147	436..2106
M453	INDO: indoleamine-pyrrole 2, 3 dioxygenase	148	149	23..1234
OV73	IPT: tRNA isopentenylpyrophosphate transferase, variant 1	150	151	15..1418
M610	IPT: tRNA isopentenylpyrophosphate transferase, variant 2	152	153	15..1418
M454	ITGA3: integrin, alpha 3	154	155	74..3274
OV30	ITGB8: integrin, beta 8	156	157	681..2990
OV34	KIAA0762: KIAA0762 protein	158	159	<1..1875
M455	KIAA0869: KIAA0869 protein	160	161	<1..2668
OV35	KIAA1154: KIAA1154 protein	162	163	<1..677
OV36	KIAA1456: KIAA1456 protein	164	165	<366..1631
OV32	KLK10: kallikrein 10	166	167	82..912
OV33	KLK6: kallikrein 6	168	169	246..980
M456	KRT7: keratin 7, variant 1	170	171	57..1466
M611	KRT7: keratin 7, variant 2	172	173	54..1463
OV53	LC27: Putative integral membrane transporter	174	175	204..1055
OV37	LCN2: Lipocalin 2 (oncogene 24p3)	176	177	1..597
M457	LEFTB: left-right determination, factor B	178	179	71..1171
M559	LPHB: lipophilin B (uteroglobin family member), prostatein-like	180	181	64..336
OV38	LYST-interacting protein LIP6	182	183	11..586
OV39	MEIS1: MEIS1 protein	184	185	66..1238
M458	MGB2: mammaglobin 2	186	187	65..352
M459	MGC3184: similar to sialyltransferase 7 ((alpha-N-acetylneuraminyl 2, 3-betagalactosyl-1, 3)-N-acetyl galactosaminide alpha-2, 6-sialyltransferase) E	188	189	176..1186
OV52	MMP7: Matrix metalloproteinase 7 (matrilysin, uterine)	190	191	28..831
OV68	MSLN: mesothelin, variant 1	192	193	88..2196
OV69	MSLN: mesothelin, variant 2	194	195	88..1980
OV70	MSLN: mesothelin, variant 3	196	197	88..1950
OV71	MSLN: mesothelin, variant 4	198	199	88..2172
OV72	MSLN: mesothelin, variant 5	200	201	88..1926
OV41	MSLN: mesothelin, variant 6	202	203	<1..>1195
OV42	MSLN: mesothelin, variant 7	204	205	85..1953
OV43	MSLN: mesothelin, variant 8	206	205	88..1956
OV44	MSLN: mesothelin, variant 9	207	208	89..1975
OV83	MSLN: mesothelin, variant 10	209	210	295..2187
OV45	MUC1: mucin 1	211	212	58..1605
M460	MUC16: mucin 16, variant 1	213	214	<1..5352
M461	MUC16: mucin 16, variant 2	215	216	25..3471
M612	MUC16: mucin 16, variant 3	215	217	<1..5673
M462	MYOM2: myomesin (M-protein)	218	219	49..4446
M463	NaPi-IIb: sodium dependent phosphate transporter isoform	220	221	36..2105
M464	NME5: protein expressed in non-metastatic cells 5	222	223	15..653

OV47	NUFIP1: nuclear fragile X mental retardation protein interacting protein 1	224	225	1..1488
OV48	OPN-a: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	226	227	1..942
OV49	OPN-b: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	228	229	88..990
OV50	OPN-c: Secreted phosphoprotein-1 (osteopontin, bone sialoprotein)	230	231	1..861
M578	PAEP: progestagen-associated endometrial protein, variant 1	232	233	36..578
M579	PAEP: progestagen-associated endometrial protein, variant 2	234	233	36..578
M580	PAEP: progestagen-associated endometrial protein, variant 3	235	233	36..578
M581	PAEP: progestagen-associated endometrial protein, variant 4	236	233	36..578
M583	PAEP: progestagen-associated endometrial protein, variant 5	237	238	45..305
M582	PAEP: progestagen-associated endometrial protein, variant 6	239	240	45..521
M613	PAEP: progestagen-associated endometrial protein, variant 7	239	241	45..521
M465	PAX8: paired box gene 8, isoform 8A	242	243	11..1363
M466	PAX8: paired box gene 8, isoform 8B, variant 1	244	245	11..1174
M614	PAX8: paired box gene 8, isoform 8B, variant 2	244	246	11..1174
M467	PAX8: paired box gene 8, isoform 8C	247	248	161..1357
M468	PAX8: paired box gene 8, isoform 8D	249	250	161..1126
M469	PAX8: paired box gene 8, isoform 8E	251	252	161..1024
M470	PRAME: preferentially expressed antigen in melanoma	253	254	236..1765
M615	PRKCI: protein kinase C, iota	255	256	205..1968
M605	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 1	257	258	<1..3133
M606	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 2	259	258	<1..3133
M607	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 3	260	258	<1..3133
OV80	PRSS8: prostasin	261	262	229..1260
OV51	PTGS1: prostaglandin-endoperoxide synthase 1	263	264	6..1805
M312	PTK9: protein tyrosine kinase 9	265	266	61..1113
OV54	pyruvate dehydrogenase complex component E2	267	268	49..>358
OV55	S100A1: S100 calcium-binding protein A1	269	270	114..398
M471	S100A11: S100 calcium-binding protein A11 (calgizzarin)	271	272	121..438
M68	S100A2: S100 calcium-binding protein A2	273	274	41..334
M585	S100A6: S100 calcium-binding protein A6 (calcyclin)	275	276	103..375

OV57	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 1	277	278	100..2109
OV85	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 2	279	280	96..2105
M472	secreted protein (HETKL27)	281	282	88..618
M473	SEMA3A: sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	283	284	16..2331
OV2	SERPINA1: alpha-1 antitrypsin	285	286	35..1291
M474	Similar to hypothetical protein, MGC: 7199	287	288	173..1053
M586	Similar to proteasome (prosome, macropain) subunit, alpha type, 3	289	290	45..791
M587	Similar to zinc finger protein 136	291	292	139..1524
M475	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 1	293	294	271..447
M185	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 2	295	296	19..417
OV60	SNCG: synuclein, gamma	297	298	49..432
OV59	SORL1: sortilin-related receptor	299	300	198..6842
OV56	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 1	301	302	301..1059
OV84	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 2	303	304	332..919
OV65	SPON1: VSGP/F-spondin, variant 1	305	306	25..2448
M593	SPON1: VSGP/F-spondin, variant 2	307	308	180..2984
M594	SPON1: VSGP/F-spondin, variant 3	309	310	180..2687
OV82	ST14: matriptase	311	312	209..2557
M476	TACSTD2: tumor-associated calcium signal transducer 2	313	314	616..1587
M588	TFPI2: tissue factor pathway inhibitor 2	315	316	57..764
OV86	TMPRSS4: transmembrane protease, serine 4	317	318	310..1623
OV74	TPH: tryptophan hydroxylase, variant 1	319	320	1..1335
OV75	TPH: tryptophan hydroxylase, variant 2	321	322	1..1401
M327	TSPAN-1: Tetraspan NET-1 protein, variant 1	323	324	124..900
M328	TSPAN-1: Tetraspan NET-1 protein, variant 2	325	326	1..726
OV46	TTID: myotilin	327	328	281..1777
M589	UCH2: Ubiquitin carboxyl-terminal hydrolases family 2	329	330	551..2940
OV63	unnamed gene (1)	331	332	71..919
OV64	unnamed gene (2)	333	334	28..804
OV76	unnamed gene (3)	335	336	69..773
OV77	unnamed gene (4)	337	338	223..1284
OV78	unnamed gene (5), variant 1	339	340	84..2450
M616	unnamed gene (5), variant 2	341	342	84..2450
OV79	unnamed gene (6)	343	344	69..392
OV87	unnamed gene (7)	345	346	509..2428
OV88	unnamed gene (8)	347	348	71..919
M477	unnamed gene (9), variant 1	349	350	246..992
M617	unnamed gene (9), variant 2	349	351	246..992
M478	unnamed gene (9), variant 3	352	353	246..1004

M479	unnamed gene (9), variant 4	354	355	246..1049
M590	unnamed gene (10), variant 1	356	357	21..404
M591	unnamed gene (10), variant 2	358	357	21..404
M592	unnamed gene (10), variant 3	359	357	21..404
OV25	WFDC2: Epididymis-specific, whey-acidic protein type, four-disulfide core; putative ovarian carcinoma marker	360	361	28..405
M480	XRCC5, KU80: ATP-dependant DNA helicase II	362	363	34..2232

TABLE 2

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
M354	ARHGAP8: Rho GTPase activating protein 8, variant 3	17	18	1..2256
M608	ARHGAP8: Rho GTPase activating protein 8, variant 4	17	19	1..2157
M355	ARHGAP8: Rho GTPase activating protein 8, variant 5	20	21	<1..1314
M356	ARHGAP8: Rho GTPase activating protein 8, variant 6	22	23	1..1902
M357	ARHGAP8: Rho GTPase activating protein 8, variant 7	24	25	<1..1281
M358	ARHGAP8: Rho GTPase activating protein 8, variant 8	26	27	1..1386
M359	ARHGAP8: Rho GTPase activating protein 8, variant 9	28	29	<1..1059
OV66	CP: ceruloplasmin (ferroxidase), variant 1	54	55	1..3210
OV81	CP: ceruloplasmin (ferroxidase), variant 4	60	61	76..3348
M575	dehydrogenase	68	69	339..1364
OV67	EVI-1: Evi-1 protein, variant 1	76	77	250..2406
M440	FLJ20758: hypothetical protein FLJ20758, variant 1	96	97	<2..1270
M441	FLJ20758: hypothetical protein FLJ20758, variant 2	98	99	<2..2095
M449	HSECP1: secretory protein, variant 2	132	133	136..768
M450	HSECP1: secretory protein, variant 3	134	135	202..933
OV73	IPT: tRNA isopentenylpyrophosphate transferase, variant 1	150	151	15..1418
M610	IPT: tRNA isopentenylpyrophosphate transferase, variant 2	152	153	15..1418
M611	KRT7: keratin 7, variant 2	172	173	54..1463
OV68	MSLN: mesothelin, variant 1	192	193	88..2196
OV69	MSLN: mesothelin, variant 2	194	195	88..1980
OV70	MSLN: mesothelin, variant 3	196	197	88..1950
OV71	MSLN: mesothelin, variant 4	198	199	88..2172
OV72	MSLN: mesothelin, variant 5	200	201	88..1926
OV83	MSLN: mesothelin, variant 10	209	210	295..2187
M460	MUC16: mucin 16, variant 1	213	214	<1..5352
M583	PAEP: progestagen-associated endometrial protein, variant 5	237	238	45..305

M613	PAEP: progestagen-associated endometrial protein, variant 7	239	241	45..521
M614	PAX8: paired box gene 8, isoform 8B, variant 2	244	246	11..1174
M605	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 1	257	258	<1..3133
M606	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 2	259	258	<1..3133
M607	PRP4: serine/threonine-protein kinase PRP4 homolog, variant 3	260	258	<1..3133
OV85	SCNN1A: sodium channel, nonvoltage-gated 1 alpha, variant 2	279	280	96..2105
M475	SLPI: secretory leukocyte protease inhibitor (antileukoproteinase), variant 1	293	294	271..447
OV84	SPINT2: serine protease inhibitor, Kunitz type, 2, variant 2	303	304	332..919
M593	SPON1: VSGP/F-spondin, variant 2	307	308	180..2984
M594	SPON1: VSGP/F-spondin, variant 3	309	310	180..2687
OV82	ST14: matriptase	311	312	209..2557
OV86	TMPRSS4: transmembrane protease, serine 4	317	318	310..1623
OV74	TPH: tryptophan hydroxylase, variant 1	319	320	1..1335
OV75	TPH: tryptophan hydroxylase, variant 2	321	322	1..1401
M327	TSPAN-1: Tetraspan NET-1 protein, variant 1	323	324	124..900
M589	UCH2: Ubiquitin carboxyl-terminal hydrolases family 2	329	330	551..2940
OV76	unnamed gene (3)	335	336	69..773
OV77	unnamed gene (4)	337	338	223..1284
OV78	unnamed gene (5), variant 1	339	340	84..2450
M616	unnamed gene (5), variant 2	341	342	84..2450
OV79	unnamed gene (6)	343	344	69..392
OV87	unnamed gene (7)	345	346	509..2428
OV88	unnamed gene (8)	347	348	71..919
M477	unnamed gene (9), variant 1	349	350	246..992
M617	unnamed gene (9), variant 2	349	351	246..992
M478	unnamed gene (9), variant 3	352	353	246..1004
M479	unnamed gene (9), variant 4	354	355	246..1049

TABLE 3

Marker	Gene Name	SEQ ID NO (nts)	SEQ ID NO (AAs)	CDS
M604	CLDN10: claudin 10	48	49	36..772
OV14	EVI-1: Evi-1 protein, variant 2	78	79	250..3405
OV15	EVI-1: Evi-1 protein, variant 3	80	81	250..2433
OV16	EVI-1: Evi-1 protein, variant 4	82	83	250..3378
M576	FLJ13710: hypothetical protein FLJ13710	88	89	96..1712
M444	FLJ22316: hypothetical protein FLJ22316	104	105	508..1206
OV30	ITGB8: integrin, beta 8	156	157	681..2990
OV43	MSLN: mesothelin, variant 8	206	205	88..1956

M581	PAEP: progestagen-associated endometrial protein, variant 4	236	233	36..578
M582	PAEP: progestagen-associated endometrial protein, variant 6	239	240	45..521
M466	PAX8: paired box gene 8, isoform 8B, variant 1	244	245	11..1174
M467	PAX8: paired box gene 8, isoform 8C	247	248	161..1357
M468	PAX8: paired box gene 8, isoform 8D	249	250	161..1126
M469	PAX8: paired box gene 8, isoform 8E	251	252	161..1024
OV2	SERPINA1: alpha-1 antitrypsin	285	286	35..1291
M474	Similar to hypothetical protein, MGC: 7199	287	288	173..1053
M590	unnamed gene (10), variant 1	356	357	21..404
M591	unnamed gene (10), variant 2	358	357	21..404
M592	unnamed gene (10), variant 3	359	357	21..404

Definitions

As used herein, each of the following terms has the meaning associated with it in this section.

The articles "a" and "an" are used herein to refer to one or to more than one (*i.e.* to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

A "marker" is a gene whose altered level of expression in a tissue or cell from its expression level in normal or healthy tissue or cell is associated with a disease state, such as cancer. A "marker nucleic acid" is a nucleic acid (*e.g.*, mRNA, cDNA) encoded by or corresponding to a marker of the invention. Such marker nucleic acids can be DNA (*e.g.*, cDNA) comprising the sequences listed in Table 1 or the complement of such sequences. The marker nucleic acids also can be RNA comprising the sequences listed in Table 1 or the complement of such sequence, wherein all thymidine residues are replaced with uridine residues. A "marker protein" is a protein encoded by or corresponding to a marker of the invention. A marker protein ~~comprises the sequence~~ of any of the sequences listed in Table 1. The terms "protein" and "polypeptide' are used interchangeably.

The term "probe" refers to any molecule which is capable of selectively binding to a specifically intended target molecule, for example, a nucleotide transcript or protein encoded by or corresponding to a marker. Probes can be either synthesized by one skilled in the art, or derived from appropriate biological preparations. For purposes of detection of the target molecule, probes may be specifically designed to be

labeled, as described herein. Examples of molecules that can be utilized as probes include, but are not limited to, RNA, DNA, proteins, antibodies, and organic molecules.

An "ovary-associated" body fluid is a fluid which, when in the body of a patient, contacts or passes through ovarian cells or into which cells or proteins shed from ovarian cells *e.g*,. ovarian epithelium, are capable of passing. Exemplary ovary-associated body fluids include blood fluids, lymph, ascites, gynecological fluids, cystic fluid, urine, and fluids collected by peritoneal rinsing.

The "normal" level of expression of a marker is the level of expression of the marker in ovarian cells of a human subject or patient not afflicted with ovarian cancer

An "over-expression" or "significantly higher level of expression" of a marker refers to an expression level in a test sample that is greater than the standard error of the assay employed to assess expression, and is preferably at least twice, and more preferably three, four, five or ten times the expression level of the marker in a control sample (*e.g.*, sample from a healthy subjects not having the marker associated disease) and preferably, the average expression level of the marker in several control samples.

As used herein, the term "promoter/regulatory sequence" means a nucleic acid sequence which is required for expression of a gene product operably linked to the promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue-specific manner.

A "constitutive" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell under most or all physiological conditions of the cell.

An "inducible" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell substantially only when an inducer which corresponds to the promoter is present in the cell.

A "tissue-specific" promoter is a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a living human cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

A "transcribed polynucleotide" or “nucleotide transcript” is a polynucleotide (*e.g.* an mRNA, hnRNA, a cDNA, or an analog of such RNA or cDNA) which is complementary to or homologous with all or a portion of a mature mRNA made by transcription of a marker of the invention and normal post-transcriptional processing (*e.g.* splicing), if any, of the RNA transcript, and reverse transcription of the RNA transcript.

"Complementary" refers to the broad concept of sequence complementarity between regions of two nucleic acid strands or between two regions of the same nucleic acid strand. It is known that an adenine residue of a first nucleic acid region is capable of forming specific hydrogen bonds ("base pairing") with a residue of a second nucleic acid region which is antiparallel to the first region if the residue is thymine or uracil. Similarly, it is known that a cytosine residue of a first nucleic acid strand is capable of base pairing with a residue of a second nucleic acid strand which is antiparallel to the first strand if the residue is guanine. A first region of a nucleic acid is complementary to a second region of the same or a different nucleic acid if, when the two regions are arranged in an antiparallel fashion, at least one nucleotide residue of the first region is capable of base pairing with a residue of the second region. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, when the first and second portions are arranged in an antiparallel fashion, at least about 50%, and preferably at least about 75%, at least about 90%, or at least about 95% of the nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion. More preferably, all nucleotide residues of the first portion are capable of base pairing with nucleotide residues in the second portion.

"Homologous" as used herein, refers to nucleotide sequence similarity between two regions of the same nucleic acid strand or between regions of two different nucleic acid strands. When a nucleotide residue position in both regions is occupied by the same nucleotide residue, then the regions are homologous at that position. A first

region is homologous to a second region if at least one nucleotide residue position of each region is occupied by the same residue. Homology between two regions is expressed in terms of the proportion of nucleotide residue positions of the two regions that are occupied by the same nucleotide residue. By way of example, a region having the nucleotide sequence 5'-ATTGCC-3' and a region having the nucleotide sequence 5'-TATGGC-3' share 50% homology. Preferably, the first region comprises a first portion and the second region comprises a second portion, whereby, at least about 50%, and preferably at least about 75%, at least about 90%, or at least about 95% of the nucleotide residue positions of each of the portions are occupied by the same nucleotide residue. More preferably, all nucleotide residue positions of each of the portions are occupied by the same nucleotide residue.

A molecule is "fixed" or “affixed” to a substrate if it is covalently or non-covalently associated with the substrate such the substrate can be rinsed with a fluid (*e.g.* standard saline citrate, pH 7.4) without a substantial fraction of the molecule dissociating from the substrate.

As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in an organism found in nature.

A cancer is "inhibited" if at least one symptom of the cancer is alleviated, terminated, slowed, or prevented. As used herein, ovarian cancer is also "inhibited" if recurrence or metastasis of the cancer is reduced, slowed, delayed, or prevented.

A kit is any manufacture (*e.g.* a package or container) comprising at least one reagent, *e.g.* a probe, for specifically detecting the expression of a marker of the invention. The kit may be promoted, distributed, or sold as a unit for performing the methods of the present invention.

“Proteins of the invention” encompass marker proteins and their fragments; variant marker proteins and their fragments; peptides and polypeptides comprising an at least 15 amino acid segment of a marker or variant marker protein; and fusion proteins comprising a marker or variant marker protein, or an at least 15 amino acid segment of a marker or variant marker protein.

Unless otherwise specified herewithin, the terms "antibody" and "antibodies" broadly encompass naturally-occurring forms of antibodies (*e.g.*, IgG, IgA, IgM, IgE) and recombinant antibodies such as single-chain antibodies, chimeric and humanized antibodies and multi-specific antibodies, as well as fragments and derivatives of all of the foregoing, which fragments and derivatives have at least an antigenic binding site. Antibody derivatives may comprise a protein or chemical moiety conjugated to an antibody moiety.

Description

The present invention is based, in part, on newly identified markers which are over-expressed in ovarian cancer cells as compared to their expression in normal (*i.e.* non-cancerous) ovarian cells. The enhanced expression of one or more of these markers in ovarian cells is herein correlated with the cancerous state of the tissue. The invention provides compositions, kits, and methods for assessing the cancerous state of ovarian cells (*e.g.* cells obtained from a human, cultured human cells, archived or preserved human cells and *in vivo* cells) as well as treating patients afflicted with ovarian cancer.

The compositions, kits, and methods of the invention have the following uses, among others:

1) assessing whether a patient is afflicted with ovarian cancer;
2) assessing the stage of ovarian cancer in a human patient;
3) assessing the grade of ovarian cancer in a patient;
4) assessing the benign or malignant nature of ovarian cancer in a patient;
5) assessing the metastatic potential of ovarian cancer in a patient;
6) assessing the histological type of neoplasm (*e.g.* serous, mucinous, endometroid, or clear cell neoplasm) associated with ovarian cancer in a patient;
7) making antibodies, antibody fragments or antibody derivatives that are useful for treating ovarian cancer and/or assessing whether a patient is afflicted with ovarian cancer;

8) assessing the presence of ovarian cancer cells;

9) assessing the efficacy of one or more test compounds for inhibiting ovarian cancer in a patient;

10) assessing the efficacy of a therapy for inhibiting ovarian cancer in a patient;

11) monitoring the progression of ovarian cancer in a patient;

12) selecting a composition or therapy for inhibiting ovarian cancer in a patient;

13) treating a patient afflicted with ovarian cancer;

14) inhibiting ovarian cancer in a patient;

15) assessing the ovarian carcinogenic potential of a test compound; and

16) preventing the onset of ovarian cancer in a patient at risk for developing ovarian cancer.

The invention thus includes a method of assessing whether a patient is afflicted with ovarian cancer which includes assessing whether the patient has pre-metastasized ovarian cancer. This method comprises comparing the level of expression of a marker of the invention (listed in Table 1) in a patient sample and the normal level of expression of the marker in a control, *e.g.*, a non-ovarian cancer sample. A significantly higher level of expression of the marker in the patient sample as compared to the normal level is an indication that the patient is afflicted with ovarian cancer.

Gene delivery vehicles, host cells and compositions (all described herein) containing nucleic acids comprising the entirety, or a segment of 15 or more nucleotides, of any of the sequences listed in Tables 1-3 or the complement of such sequences, and polypeptides comprising the entirety, or a segment of 10 or more amino acids, of any of the sequences listed in Tables 1-3 are also provided by this invention.

As described herein, ovarian cancer in patients is associated with an increased level of expression of one or more markers of the invention. While, as discussed above, some of these changes in expression level result from occurrence of the ovarian cancer, others of these changes induce, maintain, and promote the cancerous state of ovarian cancer cells. Thus, ovarian cancer characterized by an increase in the level of expression of one or more markers of the invention can be inhibited by reducing

and/or interfering with the expression of the markers and/or function of the proteins encoded by those markers.

Expression of a marker of the invention can be inhibited in a number of ways generally known in the art. For example, an antisense oligonucleotide can be provided to the ovarian cancer cells in order to inhibit transcription, translation, or both, of the marker(s). Alternately, a polynucleotide encoding an antibody, an antibody derivative, or an antibody fragment which specifically binds a marker protein, and operably linked with an appropriate promoter/regulator region, can be provided to the cell in order to generate intracellular antibodies which will inhibit the function or activity of the protein. The expression and/or function of a marker may also be inhibited by treating the ovarian cancer cell with an antibody, antibody derivative or antibody fragment that specifically binds a marker protein. Using the methods described herein, a variety of molecules, particularly including molecules sufficiently small that they are able to cross the cell membrane, can be screened in order to identify molecules which inhibit expression of a marker or inhibit the function of a marker protein. The compound so identified can be provided to the patient in order to inhibit ovarian cancer cells of the patient.

Any marker or combination of markers of the invention, as well as any known markers in combination with the markers of the invention, may be used in the compositions, kits, and methods of the present invention. In general, it is preferable to use markers for which the difference between the level of expression of the marker in ovarian cancer cells and the level of expression of the same marker in normal ovarian cells is as great as possible. Although this difference can be as small as the limit of detection of the method for assessing expression of the marker, it is preferred that the difference be at least greater than the standard error of the assessment method, and preferably a difference of at least 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 15-, 20-, 25-, 100-, 500-, 1000-fold or greater than the level of expression of the same marker in normal ovarian tissue.

It is recognized that certain marker proteins are secreted from ovarian cells (*i.e.* one or both of normal and cancerous cells) to the extracellular space surrounding the cells. These markers are preferably used in certain embodiments of the compositions, kits, and methods of the invention, owing to the fact that the such marker

proteins can be detected in an ovary-associated body fluid sample, which may be more easily collected from a human patient than a tissue biopsy sample. In addition, preferred *in vivo* techniques for detection of a marker protein include introducing into a subject a labeled antibody directed against the protein. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

It is a simple matter for the skilled artisan to determine whether any particular marker protein is a secreted protein. In order to make this determination, the marker protein is expressed in, for example, a mammalian cell, preferably a human ovarian cell line, extracellular fluid is collected, and the presence or absence of the protein in the extracellular fluid is assessed (*e.g.* using a labeled antibody which binds specifically with the protein).

The following is an example of a method which can be used to detect secretion of a protein. About 8×10^5 293T cells are incubated at 37°C in wells containing growth medium (Dulbecco's modified Eagle's medium {DMEM} supplemented with 10% fetal bovine serum) under a 5% (v/v) CO_2, 95% air atmosphere to about 60-70% confluence. The cells are then transfected using a standard transfection mixture comprising 2 micrograms of DNA comprising an expression vector encoding the protein and 10 microliters of LipofectAMINE™ (GIBCO/BRL Catalog no. 18342-012) per well. The transfection mixture is maintained for about 5 hours, and then replaced with fresh growth medium and maintained in an air atmosphere. Each well is gently rinsed twice with DMEM which does not contain methionine or cysteine (DMEM-MC; ICN Catalog no. 16-424- 54). About 1 milliliter of DMEM-MC and about 50 microcuries of Trans-^{35}S™ reagent (ICN Catalog no. 51006) are added to each well. The wells are maintained under the 5% CO_2 atmosphere described above and incubated at 37°C for a selected period. Following incubation, 150 microliters of conditioned medium is removed and centrifuged to remove floating cells and debris. The presence of the protein in the supernatant is an indication that the protein is secreted.

Examples of ovary-associated body fluids include blood fluids (*e.g.* whole blood, blood serum, blood having platelets removed therefrom, etc.), lymph, ascitic fluids, gynecological fluids (*e.g.* ovarian, fallopian, and uterine secretions, menses, vaginal douching fluids, fluids used to rinse ovarian cell samples, etc.), cystic fluid, urine, and fluids collected by peritoneal rinsing (*e.g.* fluids applied and collected during laparoscopy or fluids instilled into and withdrawn from the peritoneal cavity of a human patient). In these embodiments, the level of expression of the marker can be assessed by assessing the amount (*e.g.* absolute amount or concentration) of the marker protein in an ovary-associated body fluid obtained from a patient. The fluid can, of course, be subjected to a variety of well-known post-collection preparative and storage techniques (*e.g.* storage, freezing, ultrafiltration, concentration, evaporation, centrifugation, etc.) prior to assessing the amount of the marker in the fluid.

Many ovary-associated body fluids (*i.e.* usually excluding urine) can have ovarian cells, *e.g.* ovarian epithelium, therein, particularly when the ovarian cells are cancerous, and, more particularly, when the ovarian cancer is metastasizing. Cell-containing fluids which can contain ovarian cancer cells include, but are not limited to, peritoneal ascites, fluids collected by peritoneal rinsing, fluids collected by uterine rinsing, uterine fluids such as uterine exudate and menses, pleural fluid, and ovarian exudates. Thus, the compositions, kits, and methods of the invention can be used to detect expression of marker proteins having at least one portion which is displayed on the surface of cells which express it. It is a simple matter for the skilled artisan to determine whether a marker protein, or a portion thereof, is exposed on the cell surface. For example, immunological methods may be used to detect such proteins on whole cells, or well known computer-based sequence analysis methods (*e.g.* the SIGNALP program; Nielsen *et al.*, 1997, *Protein Engineering* 10:1-6) may be used to predict the presence of at least one extracellular domain (*i.e.* including both secreted proteins and proteins having at least one cell-surface domain). Expression of a marker protein having at least one portion which is displayed on the surface of a cell which expresses it may be detected without necessarily lysing the cell (*e.g.* using a labeled antibody which binds specifically with a cell-surface domain of the protein).

Expression of a marker of the invention may be assessed by any of a wide variety of well known methods for detecting expression of a transcribed nucleic acid or protein. Non-limiting examples of such methods include immunological methods for detection of secreted, cell-surface, cytoplasmic, or nuclear proteins, protein purification methods, protein function or activity assays, nucleic acid hybridization methods, nucleic acid reverse transcription methods, and nucleic acid amplification methods.

In a preferred embodiment, expression of a marker is assessed using an antibody (*e.g.* a radio-labeled, chromophore-labeled, fluorophore-labeled, or enzyme-labeled antibody), an antibody derivative (*e.g.* an antibody conjugated with a substrate or with the protein or ligand of a protein-ligand pair {*e.g.* biotin-streptavidin}), or an antibody fragment (*e.g.* a single-chain antibody, an isolated antibody hypervariable domain, etc.) or derivative which binds specifically with a marker protein or fragment thereof, including a marker protein which has undergone all or a portion of its normal post-translational modification.

In another preferred embodiment, expression of a marker is assessed by preparing mRNA/cDNA (*i.e.* a transcribed polynucleotide) from cells in a patient sample, and by hybridizing the mRNA/cDNA with a reference polynucleotide which is a complement of a marker nucleic acid, or a fragment thereof. cDNA can, optionally, be amplified using any of a variety of polymerase chain reaction methods prior to hybridization with the reference polynucleotide; preferably, it is not amplified. Expression of one or more markers can likewise be detected using quantitative PCR to assess the level of expression of the marker(s). Alternatively, any of the many known methods of detecting mutations or variants (*e.g.* single nucleotide polymorphisms, deletions, etc.) of a marker of the invention may be used to detect occurrence of a marker in a patient.

In a related embodiment, a mixture of transcribed polynucleotides obtained from the sample is contacted with a substrate having fixed thereto a polynucleotide complementary to or homologous with at least a portion (*e.g.* at least 7, 10, 15, 20, 25, 30, 40, 50, 100, 500, or more nucleotide residues) of a marker nucleic acid. If polynucleotides complementary to or homologous with several marker nucleic acids are differentially detectable on the substrate (*e.g.* detectable using different

chromophores or fluorophores, or fixed to different selected positions), then the levels of expression of a plurality of markers can be assessed simultaneously using a single substrate (*e.g.* a "gene chip" microarray of polynucleotides fixed at selected positions). When a method of assessing marker expression is used which involves hybridization of one nucleic acid with another, it is preferred that the hybridization be performed under stringent hybridization conditions.

Because the compositions, kits, and methods of the invention rely on detection of a difference in expression levels of one or more markers of the invention, it is preferable that the level of expression of the marker is significantly greater than the minimum detection limit of the method used to assess expression in at least one of normal ovarian cells and cancerous ovarian cells.

It is understood that by routine screening of additional patient samples using one or more of the markers of the invention, it will be realized that certain of the markers are over-expressed in cancers of various types, including specific ovarian cancers, as well as other cancers such as breast cancer, cervical cancer, etc. For example, it will be confirmed that some of the markers of the invention are over-expressed in most (*i.e.* 50% or more) or substantially all (*i.e.* 80% or more) of ovarian cancer. Furthermore, it will be confirmed that certain of the markers of the invention are associated with ovarian cancer of various stages (*i.e.* stage I, II, III, and IV ovarian cancers, as well as subclassifications IA, IB, IC, IIA, IIB, IIC, IIIA, IIIB, and IIIC, using the FIGO Stage Grouping system for primary carcinoma of the ovary; 1987, *Am. J. Obstet. Gynecol.* 156:236), of various histologic subtypes (*e.g.* serous, mucinous, endometroid, and clear cell subtypes, as well as subclassifications and alternate classifications adenocarcinoma, papillary adenocarcinoma, papillary cystadenocarcinoma, surface papillary carcinoma, malignant adenofibroma, cystadenofibroma, adenocarcinoma, cystadenocarcinoma, adenoacanthoma, endometrioid stromal sarcoma, mesodermal (Müllerian) mixed tumor, mesonephroid tumor, malignant carcinoma, Brenner tumor, mixed epithelial tumor, and undifferentiated carcinoma, using the WHO/FIGO system for classification of malignant ovarian tumors; Scully, *Atlas of Tumor Pathology*, 3d series, Washington DC), and various grades (*i.e.* grade I {well differentiated} , grade II {moderately well differentiated}, and grade III {poorly differentiated from surrounding normal tissue}).

In addition, as a greater number of patient samples are assessed for expression of the markers of the invention and the outcomes of the individual patients from whom the samples were obtained are correlated, it will also be confirmed that increased expression of certain of the markers of the invention are strongly correlated with malignant cancers and that increased expression of other markers of the invention are strongly correlated with benign tumors. The compositions, kits, and methods of the invention are thus useful for characterizing one or more of the stage, grade, histological type, and benign/malignant nature of ovarian cancer in patients. In addition, these compositions, kits, and methods can be used to detect and differentiate epithelial, stromal, and germ cell ovarian cancers.

When the compositions, kits, and methods of the invention are used for characterizing one or more of the stage, grade, histological type, and benign/malignant nature of ovarian cancer in a patient, it is preferred that the marker or panel of markers of the invention is selected such that a positive result is obtained in at least about 20%, and preferably at least about 40%, 60%, or 80%, and more preferably in substantially all patients afflicted with an ovarian cancer of the corresponding stage, grade, histological type, or benign/malignant nature. Preferably, the marker or panel of markers of the invention is selected such that a PPV of greater than about 10% is obtained for the general population (more preferably coupled with an assay specificity greater than 99.5%).

When a plurality of markers of the invention are used in the compositions, kits, and methods of the invention, the level of expression of each marker in a patient sample can be compared with the normal level of expression of each of the plurality of markers in non-cancerous samples of the same type, either in a single reaction mixture (*i.e.* using reagents, such as different fluorescent probes, for each marker) or in individual reaction mixtures corresponding to one or more of the markers. In one embodiment, a significantly increased level of expression of more than one of the plurality of markers in the sample, relative to the corresponding normal levels, is an indication that the patient is afflicted with ovarian cancer. When a plurality of markers is used, it is preferred that 2, 3, 4, 5, 8, 10, 12, 15, 20, 30, or 50 or more individual markers be used, wherein fewer markers are preferred.

In order to maximize the sensitivity of the compositions, kits, and methods of the invention (*i.e.* by interference attributable to cells of non-ovarian origin in a patient sample), it is preferable that the marker of the invention used therein be a marker which has a restricted tissue distribution, *e.g.*, normally not expressed in a non-epithelial tissue, and more preferably a marker which is normally not expressed in a non-ovarian tissue.

Only a small number of markers are known to be associated with ovarian cancers (*e.g. AKT2*, *Ki-RAS*, *ERBB2*, *c-MYC*, *RB1*, and *TP53*; Lynch, *supra*). These markers are not, of course, included among the markers of the invention, although they may be used together with one or more markers of the invention in a panel of markers, for example. It is well known that certain types of genes, such as oncogenes, tumor suppressor genes, growth factor-like genes, protease-like genes, and protein kinase-like genes are often involved with development of cancers of various types. Thus, among the markers of the invention, use of those which correspond to proteins which resemble proteins encoded by known oncogenes and tumor suppressor genes, and those which correspond to proteins which resemble growth factors, proteases, and protein kinases are preferred.

It is recognized that the compositions, kits, and methods of the invention will be of particular utility to patients having an enhanced risk of developing ovarian cancer and their medical advisors. Patients recognized as having an enhanced risk of developing ovarian cancer include, for example, patients having a familial history of ovarian cancer, patients identified as having a mutant oncogene (*i.e.* at least one allele), and patients of advancing age (*i.e.* women older than about 50 or 60 years).

The level of expression of a marker in normal (*i.e.* non-cancerous) human ovarian tissue can be assessed in a variety of ways. In one embodiment, this normal level of expression is assessed by assessing the level of expression of the marker in a portion of ovarian cells which appears to be non-cancerous and by comparing this normal level of expression with the level of expression in a portion of the ovarian cells which is suspected of being cancerous. For example, when laparoscopy or other medical procedure, reveals the presence of a lump on one portion of a patient's ovary, but not on another portion of the same ovary or on the other ovary, the normal level of expression of a marker may be assessed using one or both or the non-affected ovary and

a non-affected portion of the affected ovary, and this normal level of expression may be compared with the level of expression of the same marker in an affected portion (*i.e.* the lump) of the affected ovary. Alternately, and particularly as further information becomes available as a result of routine performance of the methods described herein, population-average values for normal expression of the markers of the invention may be used. In other embodiments, the 'normal' level of expression of a marker may be determined by assessing expression of the marker in a patient sample obtained from a non-cancer-afflicted patient, from a patient sample obtained from a patient before the suspected onset of ovarian cancer in the patient, from archived patient samples, and the like.

The invention includes compositions, kits, and methods for assessing the presence of ovarian cancer cells in a sample (*e.g.* an archived tissue sample or a sample obtained from a patient). These compositions, kits, and methods are substantially the same as those described above, except that, where necessary, the compositions, kits, and methods are adapted for use with samples other than patient samples. For example, when the sample to be used is a parafinized, archived human tissue sample, it can be necessary to adjust the ratio of compounds in the compositions of the invention, in the kits of the invention, or the methods used to assess levels of marker expression in the sample. Such methods are well known in the art and within the skill of the ordinary artisan.

The invention includes a kit for assessing the presence of ovarian cancer cells (*e.g.* in a sample such as a patient sample). The kit comprises a plurality of reagents, each of which is capable of binding specifically with a marker nucleic acid or protein. Suitable reagents for binding with a marker protein include antibodies, antibody derivatives, antibody fragments, and the like. Suitable reagents for binding with a marker nucleic acid (*e.g.* a genomic DNA, an mRNA, a spliced mRNA, a cDNA, or the like) include complementary nucleic acids. For example, the nucleic acid reagents may include oligonucleotides (labeled or non-labeled) fixed to a substrate, labeled oligonucleotides not bound with a substrate, pairs of PCR primers, molecular beacon probes, and the like.

The kit of the invention may optionally comprise additional components useful for performing the methods of the invention. By way of example, the kit may comprise fluids (*e.g.* SSC buffer) suitable for annealing complementary nucleic acids or for binding an antibody with a protein with which it specifically binds, one or more sample compartments, an instructional material which describes performance of a method of the invention, a sample of normal ovarian cells, a sample of ovarian cancer cells, and the like.

The invention also includes a method of making an isolated hybridoma which produces an antibody useful for assessing whether patient is afflicted with an ovarian cancer. In this method, a protein or peptide comprising the entirety or a segment of a marker protein is synthesized or isolated (*e.g.* by purification from a cell in which it is expressed or by transcription and translation of a nucleic acid encoding the protein or peptide *in vivo* or *in vitro* using known methods). A vertebrate, preferably a mammal such as a mouse, rat, rabbit, or sheep, is immunized using the protein or peptide. The vertebrate may optionally (and preferably) be immunized at least one additional time with the protein or peptide, so that the vertebrate exhibits a robust immune response to the protein or peptide. Splenocytes are isolated from the immunized vertebrate and fused with an immortalized cell line to form hybridomas, using any of a variety of methods well known in the art. Hybridomas formed in this manner are then screened using standard methods to identify one or more hybridomas which produce an antibody which specifically binds with the marker protein or a fragment thereof. The invention also includes hybridomas made by this method and antibodies made using such hybridomas.

The invention also includes a method of assessing the efficacy of a test compound for inhibiting ovarian cancer cells. As described above, differences in the level of expression of the markers of the invention correlate with the cancerous state of ovarian cells. Although it is recognized that changes in the levels of expression of certain of the markers of the invention likely result from the cancerous state of ovarian cells, it is likewise recognized that changes in the levels of expression of other of the markers of the invention induce, maintain, and promote the cancerous state of those cells. Thus, compounds which inhibit an ovarian cancer in a patient will cause the level of expression of one or more of the markers of the invention to change to a level nearer

the normal level of expression for that marker (*i.e.* the level of expression for the marker in non-cancerous ovarian cells).

This method thus comprises comparing expression of a marker in a first ovarian cell sample and maintained in the presence of the test compound and expression of the marker in a second ovarian cell sample and maintained in the absence of the test compound. A significantly reduced expression of a marker of the invention in the presence of the test compound is an indication that the test compound inhibits ovarian cancer. The ovarian cell samples may, for example, be aliquots of a single sample of normal ovarian cells obtained from a patient, pooled samples of normal ovarian cells obtained from a patient, cells of a normal ovarian cell line, aliquots of a single sample of ovarian cancer cells obtained from a patient, pooled samples of ovarian cancer cells obtained from a patient, cells of an ovarian cancer cell line, or the like. In one embodiment, the samples are ovarian cancer cells obtained from a patient and a plurality of compounds known to be effective for inhibiting various ovarian cancers are tested in order to identify the compound which is likely to best inhibit the ovarian cancer in the patient.

This method may likewise be used to assess the efficacy of a therapy for inhibiting ovarian cancer in a patient. In this method, the level of expression of one or more markers of the invention in a pair of samples (one subjected to the therapy, the other not subjected to the therapy) is assessed. As with the method of assessing the efficacy of test compounds, if the therapy induces a significantly lower level of expression of a marker of the invention then the therapy is efficacious for inhibiting ovarian cancer. As above, if samples from a selected patient are used in this method, then alternative therapies can be assessed *in vitro* in order to select a therapy most likely to be efficacious for inhibiting ovarian cancer in the patient.

As described above, the cancerous state of human ovarian cells is correlated with changes in the levels of expression of the markers of the invention. The invention includes a method for assessing the human ovarian cell carcinogenic potential of a test compound. This method comprises maintaining separate aliquots of human ovarian cells in the presence and absence of the test compound. Expression of a marker of the invention in each of the aliquots is compared. A significantly higher level of expression of a marker of the invention in the aliquot maintained in the presence of the

test compound (relative to the aliquot maintained in the absence of the test compound) is an indication that the test compound possesses human ovarian cell carcinogenic potential. The relative carcinogenic potentials of various test compounds can be assessed by comparing the degree of enhancement or inhibition of the level of expression of the relevant markers, by comparing the number of markers for which the level of expression is enhanced or inhibited, or by comparing both.

Various aspects of the invention are described in further detail in the following subsections.

I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules, including nucleic acids which encode a marker protein or a portion thereof. Isolated nucleic acids of the invention also include nucleic acid molecules sufficient for use as hybridization probes to identify marker nucleic acid molecules, and fragments of marker nucleic acid molecules, *e.g.*, those suitable for use as PCR primers for the amplification or mutation of marker nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (*e.g.*, cDNA or genomic DNA) and RNA molecules (*e.g.*, mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Preferably, an "isolated" nucleic acid molecule is free of sequences (preferably protein-encoding sequences) which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated nucleic acid molecule can contain less than about 5 kB, 4 kB, 3 kB, 2 kB, 1 kB, 0.5 kB or 0.1 kB of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques,

or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention can be isolated using standard molecular biology techniques and the sequence information in the database records described herein. Using all or a portion of such nucleic acid sequences, nucleic acid molecules of the invention can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook *et al.*, ed., *Molecular Cloning: A Laboratory Manual, 2nd ed.,* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid molecule of the invention can be amplified using cDNA, mRNA, or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, nucleotides corresponding to all or a portion of a nucleic acid molecule of the invention can be prepared by standard synthetic techniques, *e.g.*, using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which has a nucleotide sequence complementary to the nucleotide sequence of a marker nucleic acid or to the nucleotide sequence of a nucleic acid encoding a marker protein. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, a nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence, wherein the full length nucleic acid sequence comprises a marker nucleic acid or which encodes a marker protein. Such nucleic acids can be used, for example, as a probe or primer. The probe/primer typically is used as one or more substantially purified oligonucleotides. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 7, preferably about 15, more preferably about 25, 50, 75, 100, 125, 150, 175, 200, 250, 300, 350, or 400 or more consecutive nucleotides of a nucleic acid of the invention.

Probes based on the sequence of a nucleic acid molecule of the invention can be used to detect transcripts or genomic sequences corresponding to one or more markers of the invention. The probe comprises a label group attached thereto, *e.g.*, a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as part of a diagnostic test kit for identifying cells or tissues which mis-express the protein, such as by measuring levels of a nucleic acid molecule encoding the protein in a sample of cells from a subject, *e.g.*, detecting mRNA levels or determining whether a gene encoding the protein has been mutated or deleted.

The invention further encompasses nucleic acid molecules that differ, due to degeneracy of the genetic code, from the nucleotide sequence of nucleic acids encoding a marker protein and thus encode the same protein.

It will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequence can exist within a population (*e.g.*, the human population). Such genetic polymorphisms can exist among individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. In addition, it will be appreciated that DNA polymorphisms that affect RNA expression levels can also exist that may affect the overall expression level of that gene (*e.g.*, by affecting regulation or degradation).

As used herein, the phrase "allelic variant" refers to a nucleotide sequence which occurs at a given locus or to a polypeptide encoded by the nucleotide sequence.

As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a polypeptide corresponding to a marker of the invention. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of a given gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid polymorphisms or variations that are the result of natural allelic variation and that do not alter the functional activity are intended to be within the scope of the invention.

In another embodiment, an isolated nucleic acid molecule of the invention is at least 7, 15, 20, 25, 30, 40, 60, 80, 100, 150, 200, 250, 300, 350, 400, 450, 550, 650, 700, 800, 900, 1000, 1200, 1400, 1600, 1800, 2000, 2200, 2400, 2600, 2800, 3000, 3500, 4000, 4500, or more nucleotides in length and hybridizes under stringent conditions to a marker nucleic acid or to a nucleic acid encoding a marker protein. As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in sections 6.3.1-6.3.6 of *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989). A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

In addition to naturally-occurring allelic variants of a nucleic acid molecule of the invention that can exist in the population, the skilled artisan will further appreciate that sequence changes can be introduced by mutation thereby leading to changes in the amino acid sequence of the encoded protein, without altering the biological activity of the protein encoded thereby. For example, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are not conserved or only semi-conserved among homologs of various species may be non-essential for activity and thus would be likely targets for alteration. Alternatively, amino acid residues that are conserved among the homologs of various species (*e.g.*, murine and human) may be essential for activity and thus would not be likely targets for alteration.

Accordingly, another aspect of the invention pertains to nucleic acid molecules encoding a variant marker protein that contain changes in amino acid residues that are not essential for activity. Such variant marker proteins differ in amino acid sequence from the naturally-occurring marker proteins, yet retain biological activity. In one embodiment, such a variant marker protein has an amino acid sequence that is at

least about 40% identical, 50%, 60%, 70%, 80%, 90%, 95%, or 98% identical to the amino acid sequence of a marker protein.

An isolated nucleic acid molecule encoding a variant marker protein can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of marker nucleic acids, such that one or more amino acid residue substitutions, additions, or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), non-polar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of the coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

The present invention encompasses antisense nucleic acid molecules, *i.e.*, molecules which are complementary to a sense nucleic acid of the invention, *e.g.*, complementary to the coding strand of a double-stranded marker cDNA molecule or complementary to a marker mRNA sequence. Accordingly, an antisense nucleic acid of the invention can hydrogen bond to (*i.e.* anneal with) a sense nucleic acid of the invention. The antisense nucleic acid can be complementary to an entire coding strand, or to only a portion thereof, *e.g.*, all or part of the protein coding region (or open reading frame). An antisense nucleic acid molecule can also be antisense to all or part of a non-coding region of the coding strand of a nucleotide sequence encoding a marker protein.

The non-coding regions ("5' and 3' untranslated regions") are the 5' and 3' sequences which flank the coding region and are not translated into amino acids.

An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50 or more nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been sub-cloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a marker protein to thereby inhibit expression of the marker, *e.g.*, by inhibiting transcription and/or translation. The

hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. Examples of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site or infusion of the antisense nucleic acid into an ovary-associated body fluid. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual α-units, the strands run parallel to each other (Gaultier *et al.*, 1987, *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.*, 1987, *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue *et al.*, 1987, *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes as described in Haselhoff and Gerlach, 1988, *Nature* 334:585-591) can be used to catalytically cleave mRNA transcripts to thereby inhibit translation of the protein encoded by the mRNA. A ribozyme having specificity for a nucleic acid molecule encoding a marker protein can be designed based upon the nucleotide sequence of a cDNA corresponding to the marker. For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved

(see Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742). Alternatively, an mRNA encoding a polypeptide of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules (see, *e.g.*, Bartel and Szostak, 1993, *Science* 261:1411-1418).

The invention also encompasses nucleic acid molecules which form triple helical structures. For example, expression of a marker of the invention can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the gene encoding the marker nucleic acid or protein (*e.g.*, the promoter and/or enhancer) to form triple helical structures that prevent transcription of the gene in target cells. See generally Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

In various embodiments, the nucleic acid molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.*, 1996, *Bioorganic & Medicinal Chemistry* 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996), *supra*; Perry-O'Keefe *et al.* (1996) *Proc. Natl. Acad. Sci. USA* 93:14670-675.

PNAs can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup (1996), *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup, 1996, *supra*; Perry-O'Keefe *et al.*, 1996, *Proc. Natl. Acad. Sci. USA* 93:14670-675).

In another embodiment, PNAs can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated which can combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup, 1996, *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996), *supra,* and Finn *et al.* (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag *et al.*, 1989, *Nucleic Acids Res.* 17:5973-88). PNA monomers are then coupled in a step-wise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.*, 1996, *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser *et al.*, 1975, *Bioorganic Med. Chem. Lett.* 5:1119-11124).

In other embodiments, the oligonucleotide can include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre *et al.*, 1987, *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. WO 88/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, *e.g.*, Krol *et al.*, 1988, *Bio/Techniques* 6:958-976) or intercalating agents (see, *e.g.*, Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide can be conjugated to another molecule, *e.g.*, a peptide, hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The invention also includes molecular beacon nucleic acids having at least one region which is complementary to a nucleic acid of the invention, such that the molecular beacon is useful for quantitating the presence of the nucleic acid of the invention in a sample. A "molecular beacon" nucleic acid is a nucleic acid comprising a pair of complementary regions and having a fluorophore and a fluorescent quencher associated therewith. The fluorophore and quencher are associated with different portions of the nucleic acid in such an orientation that when the complementary regions are annealed with one another, fluorescence of the fluorophore is quenched by the quencher. When the complementary regions of the nucleic acid are not annealed with one another, fluorescence of the fluorophore is quenched to a lesser degree. Molecular beacon nucleic acids are described, for example, in U.S. Patent 5,876,930.

II. Isolated Proteins and Antibodies

One aspect of the invention pertains to isolated marker proteins and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise antibodies directed against a marker protein or a fragment thereof. In one embodiment, the native marker protein can be isolated from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, a protein or peptide comprising the whole or a segment of the marker protein is produced by recombinant DNA techniques. Alternative to recombinant expression, such protein or peptide can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of protein in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, protein that is substantially free of cellular material includes preparations of protein having less than about 30%, 20%, 10%, or 5% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein"). When the protein or biologically active portion thereof is recombinantly produced, it is

also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When the protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of the protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the polypeptide of interest.

Biologically active portions of a marker protein include polypeptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the marker protein, which include fewer amino acids than the full length protein, and exhibit at least one activity of the corresponding full-length protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the corresponding full-length protein. A biologically active portion of a marker protein of the invention can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length. Moreover, other biologically active portions, in which other regions of the marker protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of the native form of the marker protein.

Preferred marker proteins are encoded by nucleotide sequences comprising the sequences listed in Tables 1-3. Other useful proteins are substantially identical (*e.g.*, at least about 40%, preferably 50%, 60%, 70%, 80%, 90%, 95%, or 99%) to one of these sequences and retain the functional activity of the corresponding naturally-occurring marker protein yet differ in amino acid sequence due to natural allelic variation or mutagenesis.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences

is a function of the number of identical positions shared by the sequences (*i.e.*, % identity = # of identical positions/total # of positions (*e.g.*, overlapping positions) x100). In one embodiment the two sequences are the same length.

The determination of percent identity between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990) *Proc. Natl. Acad. Sci. USA* 87:2264-2268, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5877. Such an algorithm is incorporated into the BLASTN and BLASTX programs of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-410. BLAST nucleotide searches can be performed with the BLASTN program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to a nucleic acid molecules of the invention. BLAST protein searches can be performed with the BLASTP program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to a protein molecules of the invention. To obtain gapped alignments for comparison purposes, a newer version of the BLAST algorithm called Gapped BLAST can be utilized as described in Altschul *et al.* (1997) *Nucleic Acids Res.* 25:3389-3402, which is able to perform gapped local alignments for the programs BLASTN, BLASTP and BLASTX. Alternatively, PSI-Blast can be used to perform an iterated search which detects distant relationships between molecules. When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (*e.g.*, BLASTX and BLASTN) can be used. Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, (1988) *CABIOS* 4:11-17. Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used. Yet another useful algorithm for identifying regions of local sequence similarity and alignment is the FASTA algorithm as described in Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85:2444-2448. When using the FASTA algorithm for comparing nucleotide or amino acid sequences, a PAM120 weight residue table can, for example, be used with a *k*-tuple value of 2.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, only exact matches are counted.

The invention also provides chimeric or fusion proteins comprising a marker protein or a segment thereof. As used herein, a "chimeric protein" or "fusion protein" comprises all or part (preferably a biologically active part) of a marker protein operably linked to a heterologous polypeptide (*i.e.*, a polypeptide other than the marker protein). Within the fusion protein, the term "operably linked" is intended to indicate that the marker protein or segment thereof and the heterologous polypeptide are fused in-frame to each other. The heterologous polypeptide can be fused to the amino-terminus or the carboxyl-terminus of the marker protein or segment.

One useful fusion protein is a GST fusion protein in which a marker protein or segment is fused to the carboxyl terminus of GST sequences. Such fusion proteins can facilitate the purification of a recombinant polypeptide of the invention.

In another embodiment, the fusion protein contains a heterologous signal sequence at its amino terminus. For example, the native signal sequence of a marker protein can be removed and replaced with a signal sequence from another protein. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, 1992). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook *et al., supra*) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an immunoglobulin fusion protein in which all or part of a marker protein is fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand (soluble or membrane-bound) and a protein on the surface of a cell (receptor), to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion protein can be used to affect the bioavailability of a

cognate ligand of a marker protein. Inhibition of ligand/receptor interaction can be useful therapeutically, both for treating proliferative and differentiative disorders and for modulating (*e.g.* promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies directed against a marker protein in a subject, to purify ligands and in screening assays to identify molecules which inhibit the interaction of the marker protein with ligands.

Chimeric and fusion proteins of the invention can be produced by standard recombinant DNA techniques. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and re-amplified to generate a chimeric gene sequence (see, *e.g.*, Ausubel *et al.*, *supra*). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the polypeptide of the invention.

A signal sequence can be used to facilitate secretion and isolation of marker proteins. Signal sequences are typically characterized by a core of hydrophobic amino acids which are generally cleaved from the mature protein during secretion in one or more cleavage events. Such signal peptides contain processing sites that allow cleavage of the signal sequence from the mature proteins as they pass through the secretory pathway. Thus, the invention pertains to marker proteins, fusion proteins or segments thereof having a signal sequence, as well as to such proteins from which the signal sequence has been proteolytically cleaved (*i.e.*, the cleavage products). In one embodiment, a nucleic acid sequence encoding a signal sequence can be operably linked in an expression vector to a protein of interest, such as a marker protein or a segment thereof. The signal sequence directs secretion of the protein, such as from a eukaryotic host into which the expression vector is transformed, and the signal sequence is subsequently or concurrently cleaved. The protein can then be readily purified from the extracellular medium by art recognized methods. Alternatively, the signal sequence can

be linked to the protein of interest using a sequence which facilitates purification, such as with a GST domain.

The present invention also pertains to variants of the marker proteins. Such variants have an altered amino acid sequence which can function as either agonists (mimetics) or as antagonists. Variants can be generated by mutagenesis, *e.g.*, discrete point mutation or truncation. An agonist can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the protein. An antagonist of a protein can inhibit one or more of the activities of the naturally occurring form of the protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the protein of interest. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer side effects in a subject relative to treatment with the naturally occurring form of the protein.

Variants of a marker protein which function as either agonists (mimetics) or as antagonists can be identified by screening combinatorial libraries of mutants, *e.g.*, truncation mutants, of the protein of the invention for agonist or antagonist activity. In one embodiment, a variegated library of variants is generated by combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a degenerate set of potential protein sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (*e.g.*, for phage display). There are a variety of methods which can be used to produce libraries of potential variants of the marker proteins from a degenerate oligonucleotide sequence. Methods for synthesizing degenerate oligonucleotides are known in the art (see, *e.g.*, Narang, 1983, *Tetrahedron* 39:3; Itakura *et al.*, 1984, *Annu. Rev. Biochem.* 53:323; Itakura *et al.*, 1984, *Science* 198:1056; Ike *et al.*, 1983 *Nucleic Acid Res.* 11:477).

In addition, libraries of segments of a marker protein can be used to generate a variegated population of polypeptides for screening and subsequent selection of variant marker proteins or segments thereof. For example, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of the

coding sequence of interest with a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes amino terminal and internal fragments of various sizes of the protein of interest.

Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors, transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify variants of a protein of the invention (Arkin and Yourvan, 1992, *Proc. Natl. Acad. Sci. USA* *89*:7811-7815; Delgrave *et al.*, 1993, *Protein Engineering* 6(3):327-331).

Another aspect of the invention pertains to antibodies directed against a protein of the invention. In preferred embodiments, the antibodies specifically bind a marker protein or a fragment thereof. The terms "antibody" and "antibodies" as used interchangeably herein refer to immunoglobulin molecules as well as fragments and derivatives thereof that comprise an immunologically active portion of an immunoglobulin molecule, (*i.e.*, such a portion contains an antigen binding site which specifically binds an antigen, such as a marker protein, *e.g.*, an epitope of a marker protein). An antibody which specifically binds to a protein of the invention is an antibody which binds the protein, but does not substantially bind other molecules in a sample, *e.g.*, a biological sample, which naturally contains the protein. Examples of an immunologically active portion of an immunoglobulin molecule include, but are not limited to, single-chain antibodies (scAb), F(ab) and $F(ab')_2$ fragments.

An isolated protein of the invention or a fragment thereof can be used as an immunogen to generate antibodies. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments for use as immunogens. The antigenic peptide of a protein of the invention comprises at least 8 (preferably 10, 15, 20, or 30 or more) amino acid residues of the amino acid sequence of one of the proteins of the invention, and encompasses at least one epitope of the protein such that an antibody raised against the peptide forms a specific immune complex with the protein. Preferred epitopes encompassed by the antigenic peptide are regions that are located on the surface of the protein, *e.g.*, hydrophilic regions. Hydrophobicity sequence analysis, hydrophilicity sequence analysis, or similar analyses can be used to identify hydrophilic regions. In preferred embodiments, an isolated marker protein or fragment thereof is used as an immunogen.

An immunogen typically is used to prepare antibodies by immunizing a suitable (*i.e.* immunocompetent) subject such as a rabbit, goat, mouse, or other mammal or vertebrate. An appropriate immunogenic preparation can contain, for example, recombinantly-expressed or chemically-synthesized protein or peptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or a similar immunostimulatory agent. Preferred immunogen compositions are those that contain no other human proteins such as, for example, immunogen compositions made using a non-human host cell for recombinant expression of a protein of the invention. In such a manner, the resulting antibody compositions have reduced or no binding of human proteins other than a protein of the invention.

The invention provides polyclonal and monoclonal antibodies. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a particular epitope. Preferred polyclonal and monoclonal antibody compositions are ones that have been selected for antibodies directed against a protein of the invention. Particularly preferred polyclonal and monoclonal antibody preparations are ones that contain only antibodies directed against a marker protein or fragment thereof.

Polyclonal antibodies can be prepared by immunizing a suitable subject with a protein of the invention as an immunogen The antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized polypeptide.At an appropriate time after immunization, *e.g.*, when the specific antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies (mAb) by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein (1975) *Nature* 256:495-497, the human B cell hybridoma technique (see Kozbor *et al.,* 1983, *Immunol. Today* 4:72), the EBV-hybridoma technique (see Cole *et al.*, pp. 77-96 In *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., 1985) or trioma techniques. The technology for producing hybridomas is well known (see generally *Current Protocols in Immunology,* Coligan *et al.* ed., John Wiley & Sons, New York, 1994). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants for antibodies that bind the polypeptide of interest, *e.g.*, using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal antibody directed against a protein of the invention can be identified and isolated by screening a recombinant combinatorial immunoglobulin library (*e.g.*, an antibody phage display library) with the polypeptide of interest. Kits for generating and screening phage display libraries are commercially available (*e.g.*, the Pharmacia *Recombinant Phage Antibody System*, Catalog No. 27-9400-01; and the Stratagene *SurfZAP Phage Display Kit*, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO 92/09690; PCT Publication No. WO 90/02809; Fuchs *et al.* (1991) *Bio/Technology* 9:1370-1372; Hay *et al.* (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse *et al.* (1989) *Science* 246:1275-1281; Griffiths *et al.* (1993) *EMBO J.* 12:725-734.

The invention also provides recombinant antibodies that specifically bind a protein of the invention. In preferred embodiments, the recombinant antibodies specifically binds a marker protein or fragment thereof. Recombinant antibodies include, but are not limited to, chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, single-chain antibodies and multi-specific antibodies. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region. (See, *e.g.*, Cabilly et al., U.S. Patent No. 4,816,567; and Boss et al., U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entirety.) Single-chain antibodies have an antigen binding site and consist of single polypeptides. They can be produced by techniques known in the art, for example using methods described in Ladner *et. al* U.S. Pat. No. 4,946,778 (which is incorporated herein by reference in its entirety); Bird *et al.*, (1988) *Science* 242:423-426; Whitlow *et al.*, (1991) *Methods in Enzymology* 2:1-9; Whitlow *et al.*, (1991) *Methods in Enzymology* 2:97-105; and Huston *et al.*, (1991) *Methods in Enzymology Molecular Design and Modeling: Concepts and Applications* 203:46-88. Multi-specific antibodies are antibody molecules having at least two antigen-binding sites that specifically bind different antigens. Such molecules can be produced by techniques known in the art, for example using methods described in Segal, U.S. Patent No. 4,676,980 (the disclosure of which is incorporated herein by reference in its entirety); Holliger et al., (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448; *Whitlow et al.*, (1994) *Protein Eng.* 7:1017-1026 and U.S. Pat. No. 6,121,424.

Humanized antibodies are antibody molecules from non-human species having one or more complementarity determining regions (CDRs) from the non-human species and a framework region from a human immunoglobulin molecule. (See, *e.g.*, Queen, U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety.) Humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Application 125,023; Better *et al.* (1988) *Science* 240:1041-1043; Liu *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu

et al. (1987) *J. Immunol.* 139:3521- 3526; Sun *et al.* (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura *et al.* (1987) *Cancer Res.* 47:999-1005; Wood *et al.* (1985) *Nature* 314:446-449; and Shaw *et al.* (1988) *J. Natl. Cancer Inst.* 80:1553-1559); Morrison (1985) *Science* 229:1202-1207; Oi *et al.* (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones *et al.* (1986) *Nature* 321:552-525; Verhoeyan *et al.* (1988) *Science* 239:1534; and Beidler *et al.* (1988) *J. Immunol.* 141:4053-4060.

More particularly, humanized antibodies can be produced, for example, using transgenic mice which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, *e.g.*, all or a portion of a polypeptide corresponding to a marker of the invention. Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995) *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, *e.g.*, U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, *e.g.*, a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope (Jespers *et al.*, 1994, *Bio/technology* 12:899-903).

The antibodies of the invention can be isolated after production (*e.g.*, from the blood or serum of the subject) or synthesis and further purified by well-known techniques. For example, IgG antibodies can be purified using protein A chromatography. Antibodies specific for a protein of the invention can be selected or

(*e.g.*, partially purified) or purified by, *e.g.*, affinity chromatography. For example, a recombinantly expressed and purified (or partially purified) protein of the invention is produced as described herein, and covalently or non-covalently coupled to a solid support such as, for example, a chromatography column. The column can then be used to affinity purify antibodies specific for the proteins of the invention from a sample containing antibodies directed against a large number of different epitopes, thereby generating a substantially purified antibody composition, *i.e.*, one that is substantially free of contaminating antibodies. By a substantially purified antibody composition is meant, in this context, that the antibody sample contains at most only 30% (by dry weight) of contaminating antibodies directed against epitopes other than those of the desired protein of the invention, and preferably at most 20%, yet more preferably at most 10%, and most preferably at most 5% (by dry weight) of the sample is contaminating antibodies. A purified antibody composition means that at least 99% of the antibodies in the composition are directed against the desired protein of the invention.

In a preferred embodiment, the substantially purified antibodies of the invention may specifically bind to a signal peptide, a secreted sequence, an extracellular domain, a transmembrane or a cytoplasmic domain or cytoplasmic membrane of a protein of the invention. In a particularly preferred embodiment, the substantially purified antibodies of the invention specifically bind to a secreted sequence or an extracellular domain of the amino acid sequences of a protein of the invention. In a more preferred embodiment, the substantially purified antibodies of the invention specifically bind to a secreted sequence or an extracellular domain of the amino acid sequences of a marker protein.

An antibody directed against a protein of the invention can be used to isolate the protein by standard techniques, such as affinity chromatography or immunoprecipitation. Moreover, such an antibody can be used to detect the marker protein or fragment thereof (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the level and pattern of expression of the marker. The antibodies can also be used diagnostically to monitor protein levels in tissues or body fluids (*e.g.* in an ovary-associated body fluid) as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by the

use of an antibody derivative, which comprises an antibody of the invention coupled to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S or ^{3}H.

Antibodies of the invention may also be used as therapeutic agents in treating cancers. In a preferred embodiment, completely human antibodies of the invention are used for therapeutic treatment of human cancer patients, particularly those having an ovarian cancer. In another preferred embodiment, antibodies that bind specifically to a marker protein or fragment thereof are used for therapeutic treatment. Further, such therapeutic antibody may be an antibody derivative or immunotoxin comprising an antibody conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent or a radioactive metal ion. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include taxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (*e.g.*, vincristine and vinblastine).

The conjugated antibodies of the invention can be used for modifying a given biological response, for the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as ribosome-inhibiting protein (see Better et al., U.S. Patent No. 6,146,631, the disclosure of which is incorporated herein in its entirety), abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, .alpha.-interferon, .beta.-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophase colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

Techniques for conjugating such therapeutic moiety to antibodies are well known, see, *e.g.*, Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev., 62:119-58 (1982).

Accordingly, in one aspect, the invention provides substantially purified antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. In various embodiments, the substantially purified antibodies of the invention, or fragments or derivatives thereof, can be human, non-human, chimeric and/or humanized antibodies. In another aspect, the invention provides non-human antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. Such non-human antibodies can be goat, mouse, sheep, horse, chicken, rabbit, or rat

antibodies. Alternatively, the non-human antibodies of the invention can be chimeric and/or humanized antibodies. In addition, the non-human antibodies of the invention can be polyclonal antibodies or monoclonal antibodies. In still a further aspect, the invention provides monoclonal antibodies, antibody fragments and derivatives, all of which specifically bind to a protein of the invention and preferably, a marker protein. The monoclonal antibodies can be human, humanized, chimeric and/or non-human antibodies.

The invention also provides a kit containing an antibody of the invention conjugated to a detectable substance, and instructions for use. Still another aspect of the invention is a pharmaceutical composition comprising an antibody of the invention and a pharmaceutically acceptable carrier. In preferred embodiments, the pharmaceutical composition contains an antibody of the invention, a therapeutic moiety, and a pharmaceutically acceptable carrier.

III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to vectors, preferably expression vectors, containing a nucleic acid encoding a marker protein (or a portion of such a protein). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, namely expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (*e.g.*, replication defective

retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell. This means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (*e.g.*, in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel, *Methods in Enzymology: Gene Expression Technology* vol.185, Academic Press, San Diego, CA (1991). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (*e.g.*, tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, and the like. The expression vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein.

The recombinant expression vectors of the invention can be designed for expression of a marker protein or a segment thereof in prokaryotic (*e.g.*, *E. coli*) or eukaryotic cells (*e.g.*, insect cells {using baculovirus expression vectors}, yeast cells or mammalian cells). Suitable host cells are discussed further in Goeddel, *supra*. Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a

protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988, *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann *et al.*, 1988, *Gene* 69:301-315) and pET 11d (Studier *et al.*, p. 60-89, In *Gene Expression Technology: Methods in Enzymology* vol.185, Academic Press, San Diego, CA, 1991). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 gn10-lac fusion promoter mediated by a co-expressed viral RNA polymerase (T7 gn1). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, p. 119-128, In *Gene Expression Technology: Methods in Enzymology* vol. 185, Academic Press, San Diego, CA, 1990. Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada *et al.*, 1992, *Nucleic Acids Res.* 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the expression vector is a yeast expression vector. Examples of vectors for expression in yeast *S. cerevisiae* include pYepSec1 (Baldari *et al.*, 1987, *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz, 1982, *Cell* 30:933-943), pJRY88 (Schultz *et al.*, 1987, *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and pPicZ (Invitrogen Corp, San Diego, CA).

Alternatively, the expression vector is a baculovirus expression vector. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, Sf 9 cells) include the pAc series (Smith *et al.*, 1983, *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers, 1989, *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987, *Nature* 329:840) and pMT2PC (Kaufman *et al.*, 1987, *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook *et al.*, *supra*.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert *et al.*, 1987, *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton, 1988, *Adv. Immunol.* 43:235-275), in particular promoters of T cell receptors (Winoto and Baltimore, 1989, *EMBO J.* 8:729-733) and immunoglobulins (Banerji *et al.*, 1983, *Cell* 33:729-740; Queen and Baltimore, 1983, *Cell* 33:741-748), neuron-specific promoters (*e.g.*, the neurofilament promoter; Byrne and Ruddle, 1989, *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund *et al.*, 1985, *Science* 230:912-916), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters

(Kessel and Gruss, 1990, *Science* 249:374-379) and the α-fetoprotein promoter (Camper and Tilghman, 1989, *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to the mRNA encoding a polypeptide of the invention. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue-specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid, or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see Weintraub *et al.*, 1986, *Trends in Genetics*, Vol. 1(1).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic (*e.g.*, *E. coli*) or eukaryotic cell (*e.g.*, insect cells, yeast or mammalian cells).

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection,

lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, *et al.* (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome. In order to identify and select these integrants, a gene that encodes a selectable marker (*e.g.*, for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Cells stably transfected with the introduced nucleic acid can be identified by drug selection (*e.g.*, cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, can be used to produce a marker protein or a segment thereof. Accordingly, the invention further provides methods for producing a marker protein or a segment thereof using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of the invention (into which a recombinant expression vector encoding a marker protein or a segment thereof has been introduced) in a suitable medium such that the is produced. In another embodiment, the method further comprises isolating the a marker protein or a segment thereof from the medium or the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which a sequences encoding a marker protein or a segment thereof have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous sequences encoding a marker protein of the invention have been introduced into their genome or homologous recombinant animals in which endogenous gene(s) encoding a marker protein have been altered. Such animals are useful for studying the function and/or activity of the marker protein and for identifying and/or evaluating modulators of marker protein. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human

primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, *e.g.*, an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing a nucleic acid encoding a marker protein into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the transgene to direct expression of the polypeptide of the invention to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the Mouse Embryo*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the transgene in its genome and/or expression of mRNA encoding the transgene in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying the transgene can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a gene encoding a marker protein into which a deletion, addition or substitution has been introduced to thereby alter, *e.g.*, functionally disrupt, the gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous gene is functionally disrupted (*i.e.*, no longer encodes a

functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous gene is mutated or otherwise altered but still encodes functional protein (*e.g.*, the upstream regulatory region can be altered to thereby alter the expression of the endogenous protein). In the homologous recombination vector, the altered portion of the gene is flanked at its 5' and 3' ends by additional nucleic acid of the gene to allow for homologous recombination to occur between the exogenous gene carried by the vector and an endogenous gene in an embryonic stem cell. The additional flanking nucleic acid sequences are of sufficient length for successful homologous recombination with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, *e.g.,* Thomas and Capecchi, 1987, *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic stem cell line (*e.g.*, by electroporation) and cells in which the introduced gene has homologously recombined with the endogenous gene are selected (see, *e.g.*, Li *et al.*, 1992, *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal (*e.g.*, a mouse) to form aggregation chimeras (see, *e.g.*, Bradley, *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, Ed., IRL, Oxford, 1987, pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication NOS. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, *e.g.*, Lakso *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman *et al.*, 1991, *Science* 251:1351-1355). If a *cre/loxP* recombinase system is used to regulate expression of the

transgene, animals containing transgenes encoding both the *Cre* recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, *e.g.*, by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut *et al.* (1997) *Nature* 385:810-813 and PCT Publication NOS. WO 97/07668 and WO 97/07669.

IV. Pharmaceutical Compositions

The nucleic acid molecules, polypeptides, and antibodies (also referred to herein as "active compounds") of the invention can be incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

The invention includes methods for preparing pharmaceutical compositions for modulating the expression or activity of a marker nucleic acid or protein . Such methods comprise formulating a pharmaceutically acceptable carrier with an agent which modulates expression or activity of a marker nucleic acid or protein. Such compositions can further include additional active agents. Thus, the invention further includes methods for preparing a pharmaceutical composition by formulating a pharmaceutically acceptable carrier with an agent which modulates expression or activity of a marker nucleic acid or protein and one or more additional active compounds.

The invention also provides methods (also referred to herein as "screening assays") for identifying modulators, *i.e.,* candidate or test compounds or agents (*e.g.,* peptides, peptidomimetics, peptoids, small molecules or other drugs) which (a) bind to the marker, or (b) have a modulatory (*e.g.,* stimulatory or inhibitory) effect on the activity of the marker or, more specifically, (c) have a modulatory effect on the interactions of the marker with one or more of its natural substrates (*e.g.,* peptide, protein, hormone, co-factor, or nucleic acid), or (d) have a modulatory effect on the expression of the marker. Such assays typically comprise a reaction between the marker and one or more assay components. The other components may be either the test compound itself, or a combination of test compound and a natural binding partner of the marker.

The test compounds of the present invention may be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. Test compounds may also be obtained by any of the numerous approaches in combinatorial library methods known in the art, including: biological libraries; peptoid libraries (libraries of molecules having the functionalities of peptides, but with a novel, non-peptide backbone which are resistant to enzymatic degradation but which nevertheless remain bioactive; see, *e.g.,* Zuckermann *et al.*, 1994, *J. Med. Chem.* 37:2678-85); spatially addressable parallel solid phase or solution phase libraries; synthetic library methods requiring deconvolution; the 'one-bead one-compound' library method; and synthetic library methods using affinity chromatography selection. The biological library and peptoid library approaches are limited to peptide libraries, while the other four approaches are applicable to peptide, non-peptide oligomer or small molecule libraries of compounds (Lam, 1997, *Anticancer Drug Des.* 12:145).

Examples of methods for the synthesis of molecular libraries can be found in the art, for example in: DeWitt *et al.* (1993) *Proc. Natl. Acad. Sci. U.S.A.* 90:6909; Erb *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:11422; Zuckermann *et al.* (1994). *J. Med. Chem.* 37:2678; Cho *et al.* (1993) *Science* 261:1303; Carrell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2059; Carell *et al.* (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and in Gallop *et al.* (1994) *J. Med. Chem.* 37:1233.

Libraries of compounds may be presented in solution (*e.g.*, Houghten, 1992, *Biotechniques* 13:412-421), or on beads (Lam, 1991, *Nature* 354:82-84), chips (Fodor, 1993, *Nature* 364:555-556), bacteria and/or spores, (Ladner, USP 5,223,409), plasmids (Cull *et al*, 1992, *Proc Natl Acad Sci USA* 89:1865-1869) or on phage (Scott and Smith, 1990, *Science* 249:386-390; Devlin, 1990, *Science* 249:404-406; Cwirla *et al*, 1990, *Proc. Natl. Acad. Sci.* 87:6378-6382; Felici, 1991, *J. Mol. Biol.* 222:301-310; Ladner, *supra.*).

In one embodiment, the invention provides assays for screening candidate or test compounds which are substrates of a protein encoded by or corresponding to a marker or biologically active portion thereof. In another embodiment, the invention provides assays for screening candidate or test compounds which bind to a protein encoded by or corresponding to a marker or biologically active portion thereof. Determining the ability of the test compound to directly bind to a protein can be accomplished, for example, by coupling the compound with a radioisotope or enzymatic label such that binding of the compound to the marker can be determined by detecting the labeled marker compound in a complex. For example, compounds (*e.g.*, marker substrates) can be labeled with ^{125}I, ^{35}S, ^{14}C, or ^{3}H, either directly or indirectly, and the radioisotope detected by direct counting of radioemission or by scintillation counting. Alternatively, assay components can be enzymatically labeled with, for example, horseradish peroxidase, alkaline phosphatase, or luciferase, and the enzymatic label detected by determination of conversion of an appropriate substrate to product.

In another embodiment, the invention provides assays for screening candidate or test compounds which modulate the expression of a marker or the activity of a protein encoded by or corresponding to a marker, or a biologically active portion thereof. In all likelihood, the protein encoded by or corresponding to the marker can, *in vivo*, interact with one or more molecules, such as but not limited to, peptides, proteins, hormones, cofactors and nucleic acids. For the purposes of this discussion, such cellular and extracellular molecules are referred to herein as "binding partners" or marker "substrate".

One necessary embodiment of the invention in order to facilitate such screening is the use of a protein encoded by or corresponding to marker to identify the protein's natural *in vivo* binding partners. There are many ways to accomplish this which are known to one skilled in the art. One example is the use of the marker protein as "bait protein" in a two-hybrid assay or three-hybrid assay (see, *e.g.,* U.S. Patent No. 5,283,317; Zervos *et al,* 1993, *Cell* 72:223-232; Madura *et al,* 1993, *J. Biol. Chem.* 268:12046-12054; Bartel *et al* ,1993, *Biotechniques* 14:920-924; Iwabuchi *et al,* 1993 *Oncogene* 8:1693-1696; Brent WO94/10300) in order to identify other proteins which bind to or interact with the marker (binding partners) and, therefore, are possibly involved in the natural function of the marker. Such marker binding partners are also likely to be involved in the propagation of signals by the marker protein or downstream elements of a marker protein-mediated signaling pathway. Alternatively, such marker protein binding partners may also be found to be inhibitors of the marker protein.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that encodes a marker protein fused to a gene encoding the DNA binding domain of a known transcription factor (*e.g.,* GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo,* forming a marker-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (*e.g.,* LacZ) which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be readily detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes the protein which interacts with the marker protein.

In a further embodiment, assays may be devised through the use of the invention for the purpose of identifying compounds which modulate (*e.g.,* affect either positively or negatively) interactions between a marker protein and its substrates and/or binding partners. Such compounds can include, but are not limited to, molecules such as antibodies, peptides, hormones, oligonucleotides, nucleic acids, and analogs thereof.

Such compounds may also be obtained from any available source, including systematic libraries of natural and/or synthetic compounds. The preferred assay components for use in this embodiment is an ovarian cancer marker protein identified herein, the known binding partner and/or substrate of same, and the test compound. Test compounds can be supplied from any source.

The basic principle of the assay systems used to identify compounds that interfere with the interaction between the marker protein and its binding partner involves preparing a reaction mixture containing the marker protein and its binding partner under conditions and for a time sufficient to allow the two products to interact and bind, thus forming a complex. In order to test an agent for inhibitory activity, the reaction mixture is prepared in the presence and absence of the test compound. The test compound can be initially included in the reaction mixture, or can be added at a time subsequent to the addition of the marker protein and its binding partner. Control reaction mixtures are incubated without the test compound or with a placebo. The formation of any complexes between the marker protein and its binding partner is then detected. The formation of a complex in the control reaction, but less or no such formation in the reaction mixture containing the test compound, indicates that the compound interferes with the interaction of the marker protein and its binding partner. Conversely, the formation of more complex in the presence of compound than in the control reaction indicates that the compound may enhance interaction of the marker protein and its binding partner.

The assay for compounds that interfere with the interaction of the marker protien with its binding partner may be conducted in a heterogeneous or homogeneous format. Heterogeneous assays involve anchoring either the marker protein or its binding partner onto a solid phase and detecting complexes anchored to the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the marker proteins and the binding partners (*e.g.*, by competition) can be identified by conducting the reaction in the presence of the test substance, *i.e.*, by adding the test substance to the reaction mixture prior to or simultaneously with the marker and its interactive binding partner. Alternatively, test

compounds that disrupt preformed complexes, *e.g.*, compounds with higher binding constants that displace one of the components from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are briefly described below.

In a heterogeneous assay system, either the marker protein or its binding partner is anchored onto a solid surface or matrix, while the other corresponding non-anchored component may be labeled, either directly or indirectly. In practice, microtitre plates are often utilized for this approach. The anchored species can be immobilized by a number of methods, either non-covalent or covalent, that are typically well known to one who practices the art. Non-covalent attachment can often be accomplished simply by coating the solid surface with a solution of the marker protein or its binding partner and drying. Alternatively, an immobilized antibody specific for the assay component to be anchored can be used for this purpose. Such surfaces can often be prepared in advance and stored.

In related embodiments, a fusion protein can be provided which adds a domain that allows one or both of the assay components to be anchored to a matrix. For example, glutathione-S-transferase/marker fusion proteins or glutathione-S-transferase/binding partner can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtiter plates, which are then combined with the test compound or the test compound and either the non-adsorbed marker or its binding partner, and the mixture incubated under conditions conducive to complex formation (*e.g.*, physiological conditions). Following incubation, the beads or microtiter plate wells are washed to remove any unbound assay components, the immobilized complex assessed either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of marker binding or activity determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either a marker protein or a marker protein binding partner can be immobilized utilizing conjugation of biotin and streptavidin. Biotinylated marker protein or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of

streptavidin-coated 96 well plates (Pierce Chemical). In certain embodiments, the protein-immobilized surfaces can be prepared in advance and stored.

In order to conduct the assay, the corresponding partner of the immobilized assay component is exposed to the coated surface with or without the test compound. After the reaction is complete, unreacted assay components are removed (*e.g.*, by washing) and any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the non-immobilized component is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the non-immobilized component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; *e.g.*, using a labeled antibody specific for the initially non-immobilized species (the antibody, in turn, can be directly labeled or indirectly labeled with, *e.g.*, a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds which modulate (inhibit or enhance) complex formation or which disrupt preformed complexes can be detected.

In an alternate embodiment of the invention, a homogeneous assay may be used. This is typically a reaction, analogous to those mentioned above, which is conducted in a liquid phase in the presence or absence of the test compound. The formed complexes are then separated from unreacted components, and the amount of complex formed is determined. As mentioned for heterogeneous assay systems, the order of addition of reactants to the liquid phase can yield information about which test compounds modulate (inhibit or enhance) complex formation and which disrupt preformed complexes.

In such a homogeneous assay, the reaction products may be separated from unreacted assay components by any of a number of standard techniques, including but not limited to: differential centrifugation, chromatography, electrophoresis and immunoprecipitation. In differential centrifugation, complexes of molecules may be separated from uncomplexed molecules through a series of centrifugal steps, due to the different sedimentation equilibria of complexes based on their different sizes and densities (see, for example, Rivas, G., and Minton, A.P., *Trends Biochem Sci* 1993 Aug;18(8):284-7). Standard chromatographic techniques may also be utilized to separate complexed molecules from uncomplexed ones. For example, gel filtration

chromatography separates molecules based on size, and through the utilization of an appropriate gel filtration resin in a column format, for example, the relatively larger complex may be separated from the relatively smaller uncomplexed components. Similarly, the relatively different charge properties of the complex as compared to the uncomplexed molecules may be exploited to differentially separate the complex from the remaining individual reactants, for example through the use of ion-exchange chromatography resins. Such resins and chromatographic techniques are well known to one skilled in the art (see, *e.g.*, Heegaard, 1998, *J Mol. Recognit.* 11:141-148; Hage and Tweed, 1997, *J. Chromatogr. B. Biomed. Sci. Appl.*, 699:499-525). Gel electrophoresis may also be employed to separate complexed molecules from unbound species (see, *e.g.*, Ausubel *et al* (eds.), as described in : Current Protocols in Molecular Biology, J. Wiley & Sons, New York. 1999). In this technique, protein or nucleic acid complexes are separated based on size or charge, for example. In order to maintain the binding interaction during the electrophoretic process, nondenaturing gels in the absence of reducing agent are typically preferred, but conditions appropriate to the particular interactants will be well known to one skilled in the art. Immunoprecipitation is another common technique utilized for the isolation of a protein-protein complex from solution (see, *e.g.*, Ausubel *et al* (eds.), In: Current Protocols in Molecular Biology, J. Wiley & Sons, New York. 1999). In this technique, all proteins binding to an antibody specific to one of the binding molecules are precipitated from solution by conjugating the antibody to a polymer bead that may be readily collected by centrifugation. The bound assay components are released from the beads (through a specific proteolysis event or other technique well known in the art which will not disturb the protein-protein interaction in the complex), and a second immunoprecipitation step is performed, this time utilizing antibodies specific for the correspondingly different interacting assay component. In this manner, only formed complexes should remain attached to the beads. Variations in complex formation in both the presence and the absence of a test compound can be compared, thus offering information about the ability of the compound to modulate interactions between the marker protein and its binding partner.

Also within the scope of the present invention are methods for direct detection of interactions between the marker protein and its natural binding partner and/or a test compound in a homogeneous or heterogeneous assay system without

further sample manipulation. For example, the technique of fluorescence energy transfer may be utilized (see, *e.g.*, Lakowicz *et al*, U.S. Patent No. 5,631,169; Stavrianopoulos *et al*, U.S. Patent No. 4,868,103). Generally, this technique involves the addition of a fluorophore label on a first 'donor' molecule (*e.g.*, marker or test compound) such that its emitted fluorescent energy will be absorbed by a fluorescent label on a second, 'acceptor' molecule (*e.g.*, marker or test compound), which in turn is able to fluoresce due to the absorbed energy. Alternately, the 'donor' protein molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the 'acceptor' molecule label may be differentiated from that of the 'donor'. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, spatial relationships between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the 'acceptor' molecule label in the assay should be maximal. An FET binding event can be conveniently measured through standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter). A test substance which either enhances or hinders participation of one of the species in the preformed complex will result in the generation of a signal variant to that of background. In this way, test substances that modulate interactions between a marker and its binding partner can be identified in controlled assays.

In another embodiment, modulators of marker expression are identified in a method wherein a cell is contacted with a candidate compound and the expression of marker mRNA or protein in the cell, is determined. The level of expression of marker mRNA or protein in the presence of the candidate compound is compared to the level of expression of marker mRNA or protein in the absence of the candidate compound. The candidate compound can then be identified as a modulator of marker expression based on this comparison. For example, when expression of marker mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of marker mRNA or protein expression. Conversely, when expression of marker mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of marker mRNA or protein expression. The level of marker mRNA or protein expression

in the cells can be determined by methods described herein for detecting marker mRNA or protein.

In another aspect, the invention pertains to a combination of two or more of the assays described herein. For example, a modulating agent can be identified using a cell-based or a cell free assay, and the ability of the agent to modulate the activity of a marker protein can be further confirmed *in vivo*, *e.g.*, in a whole animal model for cellular transformation and/or tumorigenesis.

This invention further pertains to novel agents identified by the above-described screening assays. Accordingly, it is within the scope of this invention to further use an agent identified as described herein in an appropriate animal model. For example, an agent identified as described herein (*e.g.*, an marker modulating agent, an antisense marker nucleic acid molecule, an marker-specific antibody, or an marker-binding partner) can be used in an animal model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as described herein can be used in an animal model to determine the mechanism of action of such an agent. Furthermore, this invention pertains to uses of novel agents identified by the above-described screening assays for treatments as described herein.

It is understood that appropriate doses of small molecule agents and protein or polypeptide agents depends upon a number of factors within the knowledge of the ordinarily skilled physician, veterinarian, or researcher. The dose(s) of these agents will vary, for example, depending upon the identity, size, and condition of the subject or sample being treated, further depending upon the route by which the composition is to be administered, if applicable, and the effect which the practitioner desires the agent to have upon the nucleic acid or polypeptide of the invention. Exemplary doses of a small molecule include milligram or microgram amounts per kilogram of subject or sample weight (*e.g.* about 1 microgram per kilogram to about 500 milligrams per kilogram, about 100 micrograms per kilogram to about 5 milligrams per kilogram, or about 1 microgram per kilogram to about 50 micrograms per kilogram). Exemplary doses of a protein or polypeptide include gram, milligram or microgram amounts per kilogram of subject or sample weight (*e.g.* about 1 microgram per kilogram to about 5 grams per kilogram, about 100 micrograms per kilogram to about 500 milligrams per kilogram, or about 1 milligram per kilogram to about 50 milligrams per kilogram). It is furthermore

understood that appropriate doses of one of these agents depend upon the potency of the agent with respect to the expression or activity to be modulated. Such appropriate doses can be determined using the assays described herein. When one or more of these agents is to be administered to an animal (*e.g.* a human) in order to modulate expression or activity of a polypeptide or nucleic acid of the invention, a physician, veterinarian, or researcher can, for example, prescribe a relatively low dose at first, subsequently increasing the dose until an appropriate response is obtained. In addition, it is understood that the specific dose level for any particular animal subject will depend upon a variety of factors including the activity of the specific agent employed, the age, body weight, general health, gender, and diet of the subject, the time of administration, the route of administration, the rate of excretion, any drug combination, and the degree of expression or activity to be modulated.

A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.*, intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediamine-tetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy

syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, or sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (*e.g.*, a polypeptide or antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium, and then incorporating the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed.

Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches, and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer.

Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to those skilled in the art. The materials can also be obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes having monoclonal antibodies incorporated therein or thereon) can also be used as pharmaceutically

acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

For antibodies, the preferred dosage is 0.1 mg/kg to 100 mg/kg of body weight (generally 10 mg/kg to 20 mg/kg). If the antibody is to act in the brain, a dosage of 50 mg/kg to 100 mg/kg is usually appropriate. Generally, partially human antibodies and fully human antibodies have a longer half-life within the human body than other antibodies. Accordingly, lower dosages and less frequent administration is often possible. Modifications such as lipidation can be used to stabilize antibodies and to enhance uptake and tissue penetration (*e.g.*, into the ovarian epithelium). A method for lipidation of antibodies is described by Cruikshank *et al.* (1997) *J. Acquired Immune Deficiency Syndromes and Human Retrovirology* 14:193.

The invention also provides vaccine compositions for the prevention and/or treatment of ovarian cancer. The invention provides ovarian cancer vaccine compositions in which a protein of a marker of Table 1, or a combination of proteins of the markers of Table 1, are introduced into a subject in order to stimulate an immune response against the ovarian cancer. The invention also provides ovarian cancer vaccine compositions in which a gene expression construct, which expresses a marker or fragment of a marker identified in Table 1, is introduced into the subject such that a protein or fragment of a protein encoded by a marker of Table 1 is produced by transfected cells in the subject at a higher than normal level and elicits an immune response.

In one embodiment, an ovarian cancer vaccine is provided and employed as an immunotherapeutic agent for the prevention of ovarian cancer. In another embodiment, an ovarian cancer vaccine is provided and employed as an immunotherapeutic agent for the treatment of ovarian cancer.

By way of example, an ovarian cancer vaccine comprised of the proteins of the markers of Table 1, may be employed for the prevention and/or treatment of ovarian cancer in a subject by administering the vaccine by a variety of routes, *e.g.*, intradermally, subcutaneously, or intramuscularly. In addition, the ovarian cancer vaccine can be administered together with adjuvants and/or immunomodulators to boost the activity of the vaccine and the subject's response. In one embodiment, devices and/or compositions containing the vaccine, suitable for sustained or intermittent release could be, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body. The ovarian cancer vaccine can be introduced along with immunomodulatory compounds, which can alter the type of immune response produced in order to produce a response which will be more effective in eliminating the cancer.

In another embodiment, an ovarian cancer vaccine comprised of an expression construct of the markers of Table 1, may be introduced by injection into muscle or by coating onto microprojectiles and using a device designed for the purpose to fire the projectiles at high speed into the skin. The cells of the subject will then express the protein(s) or fragments of proteins of the markers of Table 1 and induce an immune response. In addition, the ovarian cancer vaccine may be introduced along with expression constructs for immunomodulatory molecules, such as cytokines, which may increase the immune response or modulate the type of immune response produced in order to produce a response which will be more effective in eliminating the cancer.

The marker nucleic acid molecules of the present invention can also be inserted into vectors and used as gene therapy vectors. Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470), or by stereotactic injection (see, *e.g.*, Chen *et al.*, 1994, *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively,

where the complete gene delivery vector can be produced intact from recombinant cells, *e.g.* retroviral vectors, the pharmaceutical preparation can include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

V. Predictive Medicine

The present invention pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining the level of expression of one or more marker proteins or nucleic acids, in order to determine whether an individual is at risk of developing ovarian cancer. Such assays can be used for prognostic or predictive purposes to thereby prophylactically treat an individual prior to the onset of the cancer.

Yet another aspect of the invention pertains to monitoring the influence of agents (*e.g.*, drugs or other compounds administered either to inhibit ovarian cancer or to treat or prevent any other disorder {*i.e.* in order to understand any ovarian carcinogenic effects that such treatment may have}) on the expression or activity of a marker of the invention in clinical trials. These and other agents are described in further detail in the following sections.

A. Diagnostic Assays

An exemplary method for detecting the presence or absence of a marker protein or nucleic acid in a biological sample involves obtaining a biological sample (*e.g.* an ovary-associated body fluid) from a test subject and contacting the biological sample with a compound or an agent capable of detecting the polypeptide or nucleic acid (*e.g.*, mRNA, genomic DNA, or cDNA). The detection methods of the invention can thus be used to detect mRNA, protein, cDNA, or genomic DNA, for example, in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of a marker protein include enzyme linked immunosorbent

assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of a marker protein include introducing into a subject a labeled antibody directed against the protein or fragment thereof. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

A general principle of such diagnostic and prognostic assays involves preparing a sample or reaction mixture that may contain a marker, and a probe, under appropriate conditions and for a time sufficient to allow the marker and probe to interact and bind, thus forming a complex that can be removed and/or detected in the reaction mixture. These assays can be conducted in a variety of ways.

For example, one method to conduct such an assay would involve anchoring the marker or probe onto a solid phase support, also referred to as a substrate, and detecting target marker/probe complexes anchored on the solid phase at the end of the reaction. In one embodiment of such a method, a sample from a subject, which is to be assayed for presence and/or concentration of marker, can be anchored onto a carrier or solid phase support. In another embodiment, the reverse situation is possible, in which the probe can be anchored to a solid phase and a sample from a subject can be allowed to react as an unanchored component of the assay.

There are many established methods for anchoring assay components to a solid phase. These include, without limitation, marker or probe molecules which are immobilized through conjugation of biotin and streptavidin. Such biotinylated assay components can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques known in the art (*e.g.*, biotinylation kit, Pierce Chemicals, Rockford, IL), and immobilized in the wells of streptavidin-coated 96 well plates (Pierce Chemical). In certain embodiments, the surfaces with immobilized assay components can be prepared in advance and stored.

Other suitable carriers or solid phase supports for such assays include any material capable of binding the class of molecule to which the marker or probe belongs. Well-known supports or carriers include, but are not limited to, glass, polystyrene, nylon, polypropylene, nylon, polyethylene, dextran, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

In order to conduct assays with the above mentioned approaches, the non-immobilized component is added to the solid phase upon which the second component is anchored. After the reaction is complete, uncomplexed components may be removed (*e.g.*, by washing) under conditions such that any complexes formed will remain immobilized upon the solid phase. The detection of marker/probe complexes anchored to the solid phase can be accomplished in a number of methods outlined herein.

In a preferred embodiment, the probe, when it is the unanchored assay component, can be labeled for the purpose of detection and readout of the assay, either directly or indirectly, with detectable labels discussed herein and which are well-known to one skilled in the art.

It is also possible to directly detect marker/probe complex formation without further manipulation or labeling of either component (marker or probe), for example by utilizing the technique of fluorescence energy transfer (see, for example, Lakowicz *et al.*, U.S. Patent No. 5,631,169; Stavrianopoulos, *et al.*, U.S. Patent No. 4,868,103). A fluorophore label on the first, 'donor' molecule is selected such that, upon excitation with incident light of appropriate wavelength, its emitted fluorescent energy will be absorbed by a fluorescent label on a second 'acceptor' molecule, which in turn is able to fluoresce due to the absorbed energy. Alternately, the 'donor' protein molecule may simply utilize the natural fluorescent energy of tryptophan residues. Labels are chosen that emit different wavelengths of light, such that the 'acceptor' molecule label may be differentiated from that of the 'donor'. Since the efficiency of energy transfer between the labels is related to the distance separating the molecules, spatial relationships between the molecules can be assessed. In a situation in which binding occurs between the molecules, the fluorescent emission of the 'acceptor' molecule label in the assay should be maximal. An FET binding event can be conveniently measured through standard fluorometric detection means well known in the art (*e.g.*, using a fluorimeter).

In another embodiment, determination of the ability of a probe to recognize a marker can be accomplished without labeling either assay component (probe or marker) by utilizing a technology such as real-time Biomolecular Interaction Analysis (BIA) (see, *e.g.*, Sjolander, S. and Urbaniczky, C., 1991, *Anal. Chem.* 63:2338-2345

and Szabo *et al.*, 1995, *Curr. Opin. Struct. Biol.* 5:699-705). As used herein, "BIA" or "surface plasmon resonance" is a technology for studying biospecific interactions in real time, without labeling any of the interactants (*e.g.*, BIAcore). Changes in the mass at the binding surface (indicative of a binding event) result in alterations of the refractive index of light near the surface (the optical phenomenon of surface plasmon resonance (SPR)), resulting in a detectable signal which can be used as an indication of real-time reactions between biological molecules.

Alternatively, in another embodiment, analogous diagnostic and prognostic assays can be conducted with marker and probe as solutes in a liquid phase. In such an assay, the complexed marker and probe are separated from uncomplexed components by any of a number of standard techniques, including but not limited to: differential centrifugation, chromatography, electrophoresis and immunoprecipitation. In differential centrifugation, marker/probe complexes may be separated from uncomplexed assay components through a series of centrifugal steps, due to the different sedimentation equilibria of complexes based on their different sizes and densities (see, for example, Rivas, G., and Minton, A.P., 1993, *Trends Biochem Sci.* 18(8):284-7). Standard chromatographic techniques may also be utilized to separate complexed molecules from uncomplexed ones. For example, gel filtration chromatography separates molecules based on size, and through the utilization of an appropriate gel filtration resin in a column format, for example, the relatively larger complex may be separated from the relatively smaller uncomplexed components. Similarly, the relatively different charge properties of the marker/probe complex as compared to the uncomplexed components may be exploited to differentiate the complex from uncomplexed components, for example through the utilization of ion-exchange chromatography resins. Such resins and chromatographic techniques are well known to one skilled in the art (see, *e.g.*, Heegaard, N.H., 1998, *J. Mol. Recognit.* Winter 11(1-6):141-8; Hage, D.S., and Tweed, S.A. *J Chromatogr B Biomed Sci Appl* 1997 Oct 10;699(1-2):499-525). Gel electrophoresis may also be employed to separate complexed assay components from unbound components (see, *e.g.*, Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, 1987-1999). In this technique, protein or nucleic acid complexes are separated based on size or charge, for example. In order to maintain the binding interaction during the

electrophoretic process, non-denaturing gel matrix materials and conditions in the absence of reducing agent are typically preferred. Appropriate conditions to the particular assay and components thereof will be well known to one skilled in the art.

In a particular embodiment, the level of marker mRNA can be determined both by *in situ* and by *in vitro* formats in a biological sample using methods known in the art. The term "biological sample" is intended to include tissues, cells, biological fluids and isolates thereof, isolated from a subject, as well as tissues, cells and fluids present within a subject. Many expression detection methods use isolated RNA. For *in vitro* methods, any RNA isolation technique that does not select against the isolation of mRNA can be utilized for the purification of RNA from ovarian cells (see, *e.g.*, Ausubel *et al.*, ed., *Current Protocols in Molecular Biology*, John Wiley & Sons, New York 1987-1999). Additionally, large numbers of tissue samples can readily be processed using techniques well known to those of skill in the art, such as, for example, the single-step RNA isolation process of Chomczynski (1989, U.S. Patent No. 4,843,155).

The isolated mRNA can be used in hybridization or amplification assays that include, but are not limited to, Southern or Northern analyses, polymerase chain reaction analyses and probe arrays. One preferred diagnostic method for the detection of mRNA levels involves contacting the isolated mRNA with a nucleic acid molecule (probe) that can hybridize to the mRNA encoded by the gene being detected. The nucleic acid probe can be, for example, a full-length cDNA, or a portion thereof, such as an oligonucleotide of at least 7, 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to a mRNA or genomic DNA encoding a marker of the present invention. Other suitable probes for use in the diagnostic assays of the invention are described herein. Hybridization of an mRNA with the probe indicates that the marker in question is being expressed.

In one format, the mRNA is immobilized on a solid surface and contacted with a probe, for example by running the isolated mRNA on an agarose gel and transferring the mRNA from the gel to a membrane, such as nitrocellulose. In an alternative format, the probe(s) are immobilized on a solid surface and the mRNA is contacted with the probe(s), for example, in an Affymetrix gene chip array. A skilled

artisan can readily adapt known mRNA detection methods for use in detecting the level of mRNA encoded by the markers of the present invention.

An alternative method for determining the level of mRNA marker in a sample involves the process of nucleic acid amplification, *e.g.*, by rtPCR (the experimental embodiment set forth in Mullis, 1987, U.S. Patent No. 4,683,202), ligase chain reaction (Barany, 1991, *Proc. Natl. Acad. Sci. USA,* 88:189-193), self sustained sequence replication (Guatelli *et al.*, 1990, *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh *et al.*, 1989, *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi *et al.*, 1988, *Bio/Technology* 6:1197), rolling circle replication (Lizardi *et al.*, U.S. Patent No. 5,854,033) or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers. As used herein, amplification primers are defined as being a pair of nucleic acid molecules that can anneal to 5' or 3' regions of a gene (plus and minus strands, respectively, or vice-versa) and contain a short region in between. In general, amplification primers are from about 10 to 30 nucleotides in length and flank a region from about 50 to 200 nucleotides in length. Under appropriate conditions and with appropriate reagents, such primers permit the amplification of a nucleic acid molecule comprising the nucleotide sequence flanked by the primers.

For *in situ* methods, mRNA does not need to be isolated from the ovarian cells prior to detection. In such methods, a cell or tissue sample is prepared/processed using known histological methods. The sample is then immobilized on a support, typically a glass slide, and then contacted with a probe that can hybridize to mRNA that encodes the marker.

As an alternative to making determinations based on the absolute expression level of the marker, determinations may be based on the normalized expression level of the marker. Expression levels are normalized by correcting the absolute expression level of a marker by comparing its expression to the expression of a gene that is not a marker, *e.g.*, a housekeeping gene that is constitutively expressed. Suitable genes for normalization include housekeeping genes such as the actin gene, or epithelial cell-specific genes. This normalization allows the comparison of the

expression level in one sample, *e.g.*, a patient sample, to another sample, *e.g.*, a non-ovarian cancer sample, or between samples from different sources.

Alternatively, the expression level can be provided as a relative expression level. To determine a relative expression level of a marker, the level of expression of the marker is determined for 10 or more samples of normal versus cancer cell isolates, preferably 50 or more samples, prior to the determination of the expression level for the sample in question. The mean expression level of each of the genes assayed in the larger number of samples is determined and this is used as a baseline expression level for the marker. The expression level of the marker determined for the test sample (absolute level of expression) is then divided by the mean expression value obtained for that marker. This provides a relative expression level.

Preferably, the samples used in the baseline determination will be from ovarian cancer or from non-ovarian cancer cells of ovarian tissue. The choice of the cell source is dependent on the use of the relative expression level. Using expression found in normal tissues as a mean expression score aids in validating whether the marker assayed is ovarian specific (versus normal cells). In addition, as more data is accumulated, the mean expression value can be revised, providing improved relative expression values based on accumulated data. Expression data from ovarian cells provides a means for grading the severity of the ovarian cancer state.

In another embodiment of the present invention, a marker protein is detected. A preferred agent for detecting marker protein of the invention is an antibody capable of binding to such a protein or a fragment thereof, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment or derivatives thereof (*e.g.*, Fab or $F(ab')_2$) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin.

Proteins from ovarian cells can be isolated using techniques that are well known to those of skill in the art. The protein isolation methods employed can, for example, be such as those described in Harlow and Lane (Harlow and Lane, 1988, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York).

A variety of formats can be employed to determine whether a sample contains a protein that binds to a given antibody. Examples of such formats include, but are not limited to, enzyme immunoassay (EIA), radioimmunoassay (RIA), Western blot analysis and enzyme linked immunoabsorbant assay (ELISA). A skilled artisan can readily adapt known protein/antibody detection methods for use in determining whether ovarian cells express a marker of the present invention.

In one format, antibodies, or antibody fragments or derivatives, can be used in methods such as Western blots or immunofluorescence techniques to detect the expressed proteins. In such uses, it is generally preferable to immobilize either the antibody or proteins on a solid support. Suitable solid phase supports or carriers include any support capable of binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite.

One skilled in the art will know many other suitable carriers for binding antibody or antigen, and will be able to adapt such support for use with the present invention. For example, protein isolated from ovarian cells can be run on a polyacrylamide gel electrophoresis and immobilized onto a solid phase support such as nitrocellulose. The support can then be washed with suitable buffers followed by treatment with the detectably labeled antibody. The solid phase support can then be washed with the buffer a second time to remove unbound antibody. The amount of bound label on the solid support can then be detected by conventional means.

The invention also encompasses kits for detecting the presence of a marker protein or nucleic acid in a biological sample (*e.g.* an ovary-associated body fluid such as a urine sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing ovarian cancer. For example, the kit can comprise a labeled compound or agent capable of detecting a marker protein or nucleic acid in a biological sample and means for determining the amount of the protein or

mRNA in the sample (*e.g.*, an antibody which binds the protein or a fragment thereof, or an oligonucleotide probe which binds to DNA or mRNA encoding the protein). Kits can also include instructions for interpreting the results obtained using the kit.

For antibody-based kits, the kit can comprise, for example: (1) a first antibody (*e.g.*, attached to a solid support) which binds to a marker protein; and, optionally, (2) a second, different antibody which binds to either the protein or the first antibody and is conjugated to a detectable label.

For oligonucleotide-based kits, the kit can comprise, for example: (1) an oligonucleotide, *e.g.*, a detectably labeled oligonucleotide, which hybridizes to a nucleic acid sequence encoding a marker protein or (2) a pair of primers useful for amplifying a marker nucleic acid molecule. The kit can also comprise, *e.g.*, a buffering agent, a preservative, or a protein stabilizing agent. The kit can further comprise components necessary for detecting the detectable label (*e.g.*, an enzyme or a substrate). The kit can also contain a control sample or a series of control samples which can be assayed and compared to the test sample. Each component of the kit can be enclosed within an individual container and all of the various containers can be within a single package, along with instructions for interpreting the results of the assays performed using the kit.

B. Pharmacogenomics

Agents or modulators which have a stimulatory or inhibitory effect on expression of a marker of the invention can be administered to individuals to treat (prophylactically or therapeutically) ovarian cancer in the patient. In conjunction with such treatment, the pharmacogenomics (*i.e.*, the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (*e.g.*, drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the level of expression of a marker of the invention in an

individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, *e.g.*, Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common inherited enzymopathy in which the main clinical complication is hemolysis after ingestion of oxidant drugs (anti-malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (*e.g.*, N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, a PM will show no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the level of expression of a marker of the invention in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a modulator of expression of a marker of the invention.

C. Monitoring Clinical Trials

Monitoring the influence of agents (*e.g.*, drug compounds) on the level of expression of a marker of the invention can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent to affect marker expression can be monitored in clinical trials of subjects receiving treatment for ovarian cancer. In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (*e.g.*, an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of one or more selected markers of the invention in the pre-administration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression of the marker(s) in the post-administration samples; (v) comparing the level of expression of the marker(s) in the pre-administration sample with the level of expression of the marker(s) in the post-administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent can be desirable to increase expression of the marker(s) to higher levels than detected, *i.e.*, to increase the effectiveness of the agent. Alternatively, decreased administration of the agent can be desirable to decrease expression of the marker(s) to lower levels than detected, *i.e.*, to decrease the effectiveness of the agent.

D. Electronic Apparatus Readable Media and Arrays

Electronic apparatus readable media comprising a marker of the present invention is also provided. As used herein, "electronic apparatus readable media" refers to any suitable medium for storing, holding or containing data or information that can be read and accessed directly by an electronic apparatus. Such media can include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as compact disc; electronic storage media such as RAM, ROM, EPROM, EEPROM and the like; general hard disks and hybrids of these categories such as magnetic/optical storage media. The medium is adapted or configured for having recorded thereon a marker of the present invention.

As used herein, the term "electronic apparatus" is intended to include any suitable computing or processing apparatus or other device configured or adapted for storing data or information. Examples of electronic apparatus suitable for use with the present invention include stand-alone computing apparatus; networks, including a local area network (LAN), a wide area network (WAN) Internet, Intranet, and Extranet; electronic appliances such as a personal digital assistants (PDAs), cellular phone, pager and the like; and local and distributed processing systems.

As used herein, "recorded" refers to a process for storing or encoding information on the electronic apparatus readable medium. Those skilled in the art can readily adopt any of the presently known methods for recording information on known media to generate manufactures comprising the markers of the present invention.

A variety of software programs and formats can be used to store the marker information of the present invention on the electronic apparatus readable medium. For example, the marker nucleic acid sequence can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and MicroSoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like, as well as in other forms. Any number of data processor structuring formats (*e.g.*, text file or database) may be employed in order to obtain or create a medium having recorded thereon the the markers of the present invention.

By providing the markers of the invention in readable form, one can routinely access the marker sequence information for a variety of purposes. For example, one skilled in the art can use the nucleotide or amino acid sequences of the present invention in readable form to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of the sequences of the invention which match a particular target sequence or target motif.

The present invention therefore provides a medium for holding instructions for performing a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer, wherein the method comprises the steps of determining the presence or absence of a marker and based on the presence or absence of the marker, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer and/or recommending a particular treatment for ovarian cancer or pre-ovarian cancer condition.

The present invention further provides in an electronic system and/or in a network, a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer associated with a marker wherein the method comprises the steps of determining the presence or absence of the marker, and based on the presence or absence of the marker, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer, and/or recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition. The method may further comprise the step of receiving phenotypic information associated with the subject and/or acquiring from a network phenotypic information associated with the subject.

The present invention also provides in a network, a method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer associated with a marker, said method comprising the steps of receiving information associated with the marker receiving phenotypic information associated with the subject, acquiring information from the network corresponding to the marker and/or ovarian cancer, and based on one or more of the phenotypic information, the marker, and the acquired information, determining whether the subject has a ovarian cancer or a pre-disposition to ovarian cancer. The method may further comprise the step of

recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition.

The present invention also provides a business method for determining whether a subject has ovarian cancer or a pre-disposition to ovarian cancer, said method comprising the steps of receiving information associated with the marker, receiving phenotypic information associated with the subject, acquiring information from the network corresponding to the marker and/or ovarian cancer, and based on one or more of the phenotypic information, the marker, and the acquired information, determining whether the subject has ovarian cancer or a pre-disposition to ovarian cancer. The method may further comprise the step of recommending a particular treatment for the ovarian cancer or pre-ovarian cancer condition.

The invention also includes an array comprising a marker of the present invention. The array can be used to assay expression of one or more genes in the array. In one embodiment, the array can be used to assay gene expression in a tissue to ascertain tissue specificity of genes in the array. In this manner, up to about 7600 genes can be simultaneously assayed for expression. This allows a profile to be developed showing a battery of genes specifically expressed in one or more tissues.

In addition to such qualitative determination, the invention allows the quantitation of gene expression. Thus, not only tissue specificity, but also the level of expression of a battery of genes in the tissue is ascertainable. Thus, genes can be grouped on the basis of their tissue expression *per se* and level of expression in that tissue. This is useful, for example, in ascertaining the relationship of gene expression between or among tissues. Thus, one tissue can be perturbed and the effect on gene expression in a second tissue can be determined. In this context, the effect of one cell type on another cell type in response to a biological stimulus can be determined. Such a determination is useful, for example, to know the effect of cell-cell interaction at the level of gene expression. If an agent is administered therapeutically to treat one cell type but has an undesirable effect on another cell type, the invention provides an assay to determine the molecular basis of the undesirable effect and thus provides the opportunity to co-administer a counteracting agent or otherwise treat the undesired effect. Similarly, even within a single cell type, undesirable biological effects can be

determined at the molecular level. Thus, the effects of an agent on expression of other than the target gene can be ascertained and counteracted.

In another embodiment, the array can be used to monitor the time course of expression of one or more genes in the array. This can occur in various biological contexts, as disclosed herein, for example development of ovarian cancer, progression of ovarian cancer, and processes, such a cellular transformation associated with ovarian cancer.

The array is also useful for ascertaining the effect of the expression of a gene on the expression of other genes in the same cell or in different cells. This provides, for example, for a selection of alternate molecular targets for therapeutic intervention if the ultimate or downstream target cannot be regulated.

The array is also useful for ascertaining differential expression patterns of one or more genes in normal and abnormal cells. This provides a battery of genes that could serve as a molecular target for diagnosis or therapeutic intervention.

E. Surrogate Markers

The markers of the invention may serve as surrogate markers for one or more disorders or disease states or for conditions leading up to disease states, and in particular, ovarian cancer. As used herein, a "surrogate marker" is an objective biochemical marker which correlates with the absence or presence of a disease or disorder, or with the progression of a disease or disorder (*e.g.*, with the presence or absence of a tumor). The presence or quantity of such markers is independent of the disease. Therefore, these markers may serve to indicate whether a particular course of treatment is effective in lessening a disease state or disorder. Surrogate markers are of particular use when the presence or extent of a disease state or disorder is difficult to assess through standard methodologies (*e.g.*, early stage tumors), or when an assessment of disease progression is desired before a potentially dangerous clinical endpoint is reached (*e.g.*, an assessment of cardiovascular disease may be made using cholesterol levels as a surrogate marker, and an analysis of HIV infection may be made using HIV RNA levels as a surrogate marker, well in advance of the undesirable clinical outcomes of myocardial infarction or fully-developed AIDS). Examples of the use of surrogate

markers in the art include: Koomen *et al.* (2000) *J. Mass. Spectrom.* 35: 258-264; and James (1994) *AIDS Treatment News Archive* 209.

The markers of the invention are also useful as pharmacodynamic markers. As used herein, a "pharmacodynamic marker" is an objective biochemical marker which correlates specifically with drug effects. The presence or quantity of a pharmacodynamic marker is not related to the disease state or disorder for which the drug is being administered; therefore, the presence or quantity of the marker is indicative of the presence or activity of the drug in a subject. For example, a pharmacodynamic marker may be indicative of the concentration of the drug in a biological tissue, in that the marker is either expressed or transcribed or not expressed or transcribed in that tissue in relationship to the level of the drug. In this fashion, the distribution or uptake of the drug may be monitored by the pharmacodynamic marker. Similarly, the presence or quantity of the pharmacodynamic marker may be related to the presence or quantity of the metabolic product of a drug, such that the presence or quantity of the marker is indicative of the relative breakdown rate of the drug *in vivo*. Pharmacodynamic markers are of particular use in increasing the sensitivity of detection of drug effects, particularly when the drug is administered in low doses. Since even a small amount of a drug may be sufficient to activate multiple rounds of marker transcription or expression, the amplified marker may be in a quantity which is more readily detectable than the drug itself. Also, the marker may be more easily detected due to the nature of the marker itself; for example, using the methods described herein, antibodies may be employed in an immune-based detection system for a protein marker, or marker-specific radiolabeled probes may be used to detect a mRNA marker. Furthermore, the use of a pharmacodynamic marker may offer mechanism-based prediction of risk due to drug treatment beyond the range of possible direct observations. Examples of the use of pharmacodynamic markers in the art include: Matsuda *et al.* US 6,033,862; Hattis *et al.* (1991) *Env. Health Perspect.* 90: 229-238; Schentag (1999) *Am. J. Health-Syst. Pharm.* 56 Suppl. 3: S21-S24; and Nicolau (1999) *Am, J. Health-Syst. Pharm.* 56 Suppl. 3: S16-S20.

VI. Experimental Protocol for all OV markers and M352 - M360

A. Identification of markers

The markers of the present invention were identified by transcriptional profiling using mRNA from 9 normal ovarian epithelia, 11 stage I/II ovarian cancer tumors and 25 stage III/IV tumors. Clones having expression at least two-fold higher in ovarian tumors as compared to their expression in non-ovarian tumor tissues in at least 4 tumor samples were selected to have their protein-encoding transcript sequences determined.

B. Identification of Markers and Assembly of Their Sequences

Clones which displayed an increase in expression in ovarian tumor samples over the corresponding average expression of non-tumor samples were used for further study. Briefly, BLAST analysis, against both public and proprietary sequence databases, of EST sequences known to be associated with each clone was performed, either directly or in the context of automatically, high-stringency assembled contiguous sequences. An identification of protein sequence corresponding to the clone was accomplished by obtaining one of the following:

a) a direct match between the protein sequence and at least one EST sequence in one of its 6 possible translations;

b) a direct match between the nucleotide sequence for the mRNA corresponding to the protein sequence and at least one EST sequence;

c) a match between the protein sequence and a contiguous assembly (contig) of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations; or

d) a match between the nucleotide sequence for the mRNA corresponding to the protein sequence and a contiguous assembly of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations.

C. Identification of Markers Having Newly-Identified Nucleotide and Amino Acid Sequences.

The markers of Table 2 include newly-identified amino acid sequences. These sequences were found to be novel based on one of the following criteria:

a) the protein sequence found within available public databases was incomplete or erroneous, leading to the construction of an additional completed/corrected protein sequence that is not found as such in the public domain;

b) based on nucleotide evidence, variants of the protein sequence were additionally constructed that are not found as such in the public domain; or

c) the contig for the EST sequences did not match any known protein, so that a novel protein sequence was derived from an open reading frame of the contig.

VII. Experimental Protocol for M68, M103, M138, M185, M312, M327-M328, M400, M430-M480, M559, M571-M573, M575-M576, M578-M583, M585-594, and M604-M617

A. Identification of Markers and Assembly of Their Sequences

The markers of the present invention were identified by transcription profiling using mRNA from 67 ovarian tumors of various histotypes and stage and 96 non-ovarian tumor tissues including normal ovarian epithelium, benign conditions, other normal tissues, and other abnormal tissues. Clones having expression at least three-fold higher in at least 10% of ovarian tumors, as compared to their expression in non-ovarian tumor tissue, were designated as ovarian cancer specific markers. These cDNA clones were selected to have their protein-encoding transcript sequences determined. Briefly, BLAST analysis, against both public and proprietary sequence databases, of EST sequences known to be associated with each clone was performed, either directly or in the context of automatically, high-stringency assembled contiguous sequences. An identification of protein sequence corresponding to the clone was accomplished by obtaining one of the following:

a) a direct match between the protein sequence and at least one EST sequence in one of its 6 possible translations;

b) a direct match between the nucleotide sequence for the mRNA corresponding to the protein sequence and at least one EST sequence;

c) a match between the protein sequence and a contiguous assembly (contig) of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations; or

d) a match between the nucleotide sequence for the mRNA corresponding to the protein sequence and a contiguous assembly of the EST sequences with other available EST sequences in the databases in one of its 6 possible translations.

B. Identification of Markers Having Newly-Identified Amino Acid Sequences.

The markers of Table 2 include newly-identified amino acid sequences. These sequences were found to be novel based on one of the following criteria:

a) the protein sequence found within available public databases was incomplete or erroneous, leading to the construction of an additional completed/corrected protein sequence that is not found as such in the public domain;

b) based on nucleotide evidence, variants of the protein sequence were additionally constructed that are not found as such in the public domain; or

c) the contig for the EST sequences did not match any known protein, so that a novel protein sequence was derived from an open reading frame of the contig.

VIII. Gene Expression Analysis

Total RNA from normal human tissue was obtained from commercial sources. The integrity of the RNA was verified by agarose gel electrophoresis and ethidium bromide staining. Cell lines were purchased from ATCC and grown under the conditions recommended by ATCC. Total RNA from a number of various cell lines was prepared using commercial kits (Qiagen). First strand cDNA was prepared using oligo-dT primer and standard conditions. Each RNA preparation was treated with DNase I (Ambion) at 37°C for 1 hour.

Novel gene expression was measured by TaqMan® quantitative PCR (Perkin Elmer Applied Biosystems) in cDNA prepared from the following normal human tissues: heart, kidney, skeletal muscle, pancreas, skin, dorsal root ganglion,

breast, ovary, prostate, salivary glands, lung, colon, liver and lymph node. Figure 1 graphically represents the results of the TaqMan® expression study. The columns labelled A to V depict the expression level observed for OV88 in the following tissues:

Column A: Heart, normal tissue
Column B: Heart, CHF tissue
Column C: Kidney, normal tissue
Column D: Skeletal muscle, normal tissue
Column E: Pancreas, normal tissue
Column F: Skin, normal tissue
Column G: Dorsal root, normal tissue
Column H: Breast, normal tissue
Column I: Breast, tumor tissue
Column J Ovary, normal tissue
Column K: Ovary, tumor tissue
Column L: Prostate, normal tissue
Column M: Prostate, tumor tissue
Column N: Salivary glands, normal tissue
Column O: Lung, normal tissue
Column P: Lung, tumor tissue
Column Q: Lung, COPD tissue
Column R: Colon, IBD tissue
Column S: Liver, normal tissue
Column T: Liver fibrosis
Column U: Lymph node, normal tissue
Column V: Positive control

IX. Summary of the Data Provided in the Tables

Tables 1-3 list the markers of the present invention. In the Tables the markers are identified with a name ("Marker"), the name the gene is commonly known by, if applicable ("Gene Name"), the Sequence Listing identifier of the cDNA sequence of a nucleotide transcript encoded by or corresponding to the marker ("SEQ ID NO (nts)"), the Sequence Listing identifier of the amino acid sequence of a protein encoded

by the nucleotide transcript ("SEQ ID NO (AAs)"), and the location of the protein coding sequence within the cDNA sequence ("CDS").

Table 1 lists all of the markers of the invention, which are over-expressed in ovarian cancer cells compared to normal (*i.e.*, non-cancerous) ovarian cells and comprises markers listed in Tables 2 and 3. Table 2 lists newly-identified nucleotide and amino acid sequences useful as ovarian cancer markers. Table 3 lists newly-identified nucleotide sequences useful as ovarian cancer markers.

Other Embodiments

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims:

What is claimed:

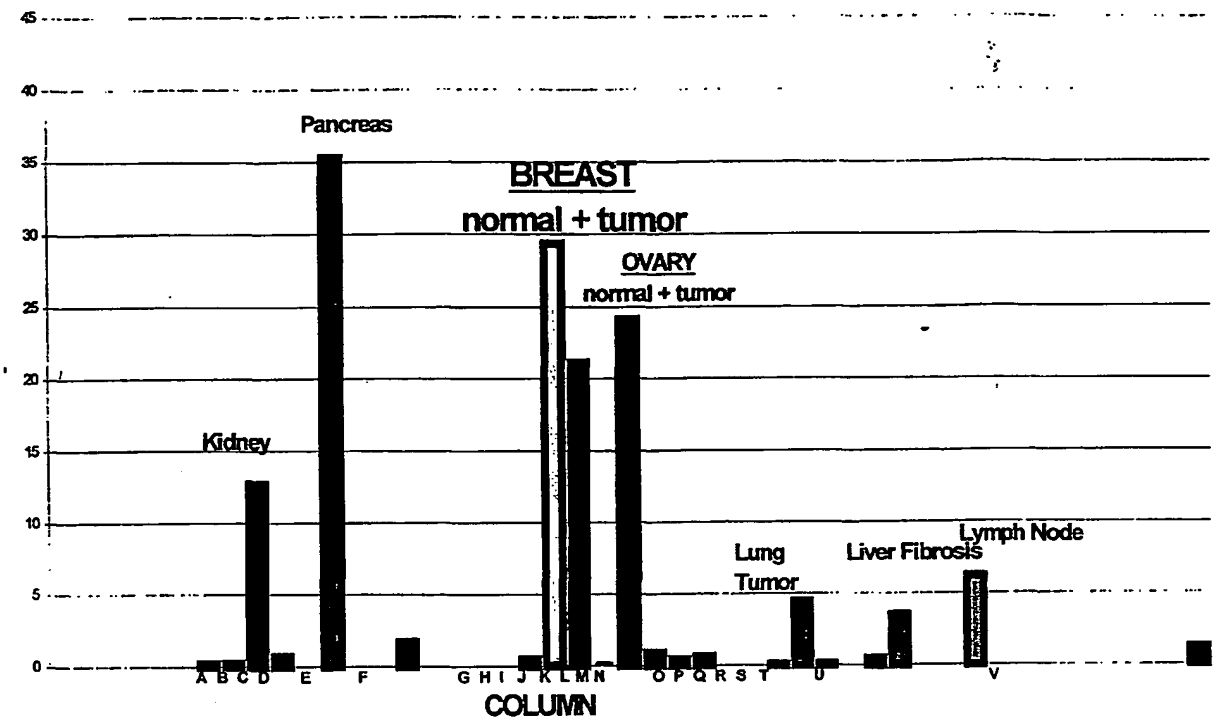
1. A method of assessing whether a patient is afflicted with ovarian cancer, the method comprising comparing:

a) the level of expression of a marker in a patient sample, wherein the marker is selected from Table 1, and

b) the normal level of expression of the marker in a control non-ovarian cancer sample,

wherein a significant increase in the level of expression of the marker in the patient sample and the normal level is an indication that the patient is afflicted with ovarian cancer.

Figure 1



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normal + tumor
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normal + tumor
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COLUMN

SEQUENCE LISTING

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Gln Lys Phe Glu His Met Tyr Ala Gln Ser Leu Gln Val Pro Tyr Arg
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Asn Ser Leu Arg Lys Ala His Ile Phe Gly Ile Thr Phe Ser Phe Thr
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945 950 955 960
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Phe Ala Pro Asp Tyr Ala Lys Ala Lys Ile Ser Ala Ala His Ile Ile
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1140 1145 1150
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1155 1160 1165
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1170 1175 1180
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<212> DNA
<213> Homo sapiens

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<210> 4
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<212> PRT
<213> Homo sapiens

<400> 4

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            20                  25                  30
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        35                  40                  45
Pro His Trp Tyr His Phe Ser Cys Phe Trp Lys Val Gly His Ser Ile
    50                  55                  60
Arg His Pro Asp Val Glu Val Asp Gly Phe Ser Glu Leu Arg Trp Asp
65                  70                  75                  80
Asp Gln Gln Lys Val Lys Lys Thr Ala Glu Ala Gly Gly Val Thr Gly
                85                  90                  95
Lys Gly Gln Asp Gly Ile Gly Ser Lys Ala Glu Lys Thr Leu Gly Asp
            100                 105                 110
Phe Ala Ala Glu Tyr Ala Lys Ser Asn Arg Ser Thr Cys Lys Gly Cys
        115                 120                 125
Met Glu Lys Ile Glu Lys Gly Gln Val Arg Leu Ser Lys Lys Met Val
    130                 135                 140
Asp Pro Glu Lys Pro Gln Leu Gly Met Ile Asp Arg Trp Tyr His Pro
145                 150                 155                 160
Gly Cys Phe Val Lys Asn Arg Glu Glu Leu Gly Phe Arg Pro Glu Tyr
                165                 170                 175
Ser Ala Ser Gln Leu Lys Gly Phe Ser Leu Leu Ala Thr Glu Asp Lys
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Glu Ala Leu Lys Lys Gln Leu Pro Gly Val Lys Ser Glu Gly Lys Arg
        195                 200                 205
Lys Gly Asp Glu Val Asp Gly Val Asp Glu Val Ala Lys Lys Lys Ser
    210                 215                 220
Lys Lys Glu Lys Asp Lys Asp Ser Lys Leu Glu Lys Ala Leu Lys Ala
225                 230                 235                 240
Gln Asn Asp Leu Ile Trp Asn Ile Lys Asp Glu Leu Lys Lys Val Cys
                245                 250                 255
Ser Thr Asn Asp Leu Lys Glu Leu Leu Ile Phe Asn Lys Gln Gln Val
            260                 265                 270
Pro Ser Gly Glu Ser Ala Ile Leu Asp Arg Val Ala Asp Gly Met Val
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Phe Gly Ala Leu Leu Pro Cys Glu Glu Cys Ser Gly Gln Leu Val Phe
    290                 295                 300
Lys Ser Asp Ala Tyr Tyr Cys Thr Gly Asp Val Thr Ala Trp Thr Lys
305                 310                 315                 320
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Cys Met Val Lys Thr Gln Thr Pro Asn Arg Lys Glu Trp Val Thr Pro
                325                 330                 335
Lys Glu Phe Arg Glu Ile Ser Tyr Leu Lys Lys Leu Lys Val Lys Lys
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Gln Asp Arg Ile Phe Pro Pro Glu Thr Ser Ala Ser Val Ala Ala Thr
        355                 360                 365
Pro Pro Pro Ser Thr Ala Ser Ala Pro Ala Ala Val Asn Ser Ser Ala
    370                 375                 380
Ser Ala Asp Lys Pro Leu Ser Asn Met Lys Ile Leu Thr Leu Gly Lys
385                 390                 395                 400
Leu Ser Arg Asn Lys Asp Glu Val Lys Ala Met Ile Glu Lys Leu Gly
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Gly Lys Leu Thr Gly Thr Ala Asn Lys Ala Ser Leu Cys Ile Ser Thr
            420                 425                 430
Lys Lys Glu Val Glu Lys Met Asn Lys Lys Met Glu Glu Val Lys Glu
        435                 440                 445
Ala Asn Ile Arg Val Val Ser Glu Asp Phe Leu Gln Asp Val Ser Ala
    450                 455                 460
Ser Thr Lys Ser Leu Gln Glu Leu Phe Leu Ala His Ile Leu Ser Pro
465                 470                 475                 480
Trp Gly Ala Glu Val Lys Ala Glu Pro Val Glu Val Val Ala Pro Arg
                485                 490                 495
Gly Lys Ser Gly Ala Ala Leu Ser Lys Lys Ser Lys Gly Gln Val Lys
            500                 505                 510
Glu Glu Gly Ile Asn Lys Ser Glu Lys Arg Met Lys Leu Thr Leu Lys
        515                 520                 525
Gly Gly Ala Ala Val Asp Pro Asp Ser Gly Leu Glu His Ser Ala His
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Val Leu Glu Lys Gly Gly Lys Val Phe Ser Ala Thr Leu Gly Leu Val
545                 550                 555                 560
Asp Ile Val Lys Gly Thr Asn Ser Tyr Tyr Lys Leu Gln Leu Leu Glu
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Asp Asp Lys Glu Asn Arg Tyr Trp Ile Phe Arg Ser Trp Gly Arg Val
            580                 585                 590
Gly Thr Val Ile Gly Ser Asn Lys Leu Glu Gln Met Pro Ser Lys Glu
        595                 600                 605
Asp Ala Ile Glu Gln Phe Met Lys Leu Tyr Glu Glu Lys Thr Gly Asn
    610                 615                 620
Ala Trp His Ser Lys Asn Phe Thr Lys Tyr Pro Lys Lys Phe Tyr Pro
625                 630                 635                 640
Leu Glu Ile Asp Tyr Gly Gln Asp Glu Glu Ala Val Lys Lys Leu Thr
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Val Asn Pro Gly Thr Lys Ser Lys Leu Pro Lys Pro Val Gln Asp Leu
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Ile Lys Met Ile Phe Asp Val Glu Ser Met Lys Lys Ala Met Val Glu
        675                 680                 685
Tyr Glu Ile Asp Leu Gln Lys Met Pro Leu Gly Lys Leu Ser Lys Arg
    690                 695                 700
Gln Ile Gln Ala Ala Tyr Ser Ile Leu Ser Glu Val Gln Gln Ala Val
705                 710                 715                 720
Ser Gln Gly Ser Ser Asp Ser Gln Ile Leu Asp Leu Ser Asn Arg Phe
                725                 730                 735
Tyr Thr Leu Ile Pro His Asp Phe Gly Met Lys Lys Pro Pro Leu Leu
            740                 745                 750
Asn Asn Ala Asp Ser Val Gln Ala Lys Val Glu Met Leu Asp Asn Leu
        755                 760                 765
Leu Asp Ile Glu Val Ala Tyr Ser Leu Leu Arg Gly Gly Ser Asp Asp
    770                 775                 780
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Ser Ser Lys Asp Pro Ile Asp Val Asn Tyr Glu Lys Leu Lys Thr Asp
785                 790                 795                 800
Ile Lys Val Val Asp Arg Asp Ser Glu Glu Ala Glu Ile Ile Arg Lys
                805                 810                 815
Tyr Val Lys Asn Thr His Ala Thr Thr His Ser Ala Tyr Asp Leu Glu
            820                 825                 830
Val Ile Asp Ile Phe Lys Ile Glu Arg Glu Gly Glu Cys Gln Arg Tyr
        835                 840                 845
Lys Pro Phe Lys Gln Leu His Asn Arg Arg Leu Leu Trp His Gly Ser
    850                 855                 860
Arg Thr Thr Asn Phe Ala Gly Ile Leu Ser Gln Gly Leu Arg Ile Ala
865                 870                 875                 880
Pro Pro Glu Ala Pro Val Thr Gly Tyr Met Phe Gly Lys Gly Ile Tyr
                885                 890                 895
Phe Ala Asp Met Val Ser Lys Ser Ala Asn Tyr Tyr His Thr Ser Gln
            900                 905                 910
Gly Asp Pro Ile Gly Leu Ile Leu Leu Gly Glu Val Ala Leu Gly Asn
        915                 920                 925
Met Tyr Glu Leu Lys His Ala Ser His Ile Ser Arg Leu Pro Lys Gly
    930                 935                 940
Lys His Ser Val Lys Gly Leu Gly Lys Thr Thr Pro Asp Pro Ser Ala
945                 950                 955                 960
Asn Ile Ser Leu Asp Gly Val Asp Val Pro Leu Gly Thr Gly Ile Ser
                965                 970                 975
Ser Gly Val Ile Asp Thr Ser Leu Leu Tyr Asn Glu Tyr Ile Val Tyr
            980                 985                 990
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Phe Lys Thr Ser Leu Trp
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<210> 5
<211> 1465
<212> DNA
<213> Homo sapiens

<400> 5

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gcgggatgct ttgaacattg aaacagccat caagaccaaa ggtgtggatg aggtcaccat 300
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<210> 6
<211> 339
<212> PRT
<213> Homo sapiens

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Phe Asp Ala Glu Arg Asp Ala Leu Asn Ile Glu Thr Ala Ile Lys Thr
35 40 45
Lys Gly Val Asp Glu Val Thr Ile Val Asn Ile Leu Thr Asn Arg Ser
50 55 60
Asn Ala Gln Arg Gln Asp Ile Ala Phe Ala Tyr Gln Arg Arg Thr Lys
65 70 75 80
Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu
85 90 95
Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser
100 105 110
Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu
115 120 125
Ile Glu Ile Ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu Ile Asn
130 135 140
Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile
145 150 155 160
Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys
165 170 175
Gly Arg Arg Ala Glu Asp Gly Ser Val Ile Asp Tyr Glu Leu Ile Asp
180 185 190
Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr
195 200 205
Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His
210 215 220
Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met
225 230 235 240
Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe
245 250 255
Leu Asn Leu Val Gln Cys Ile Gln Asn Lys Pro Leu Tyr Phe Ala Asp
260 265 270
Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu
275 280 285
Ile Arg Ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg
290 295 300
Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln
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325 330 335
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<211> 1362
<212> DNA
<213> Homo sapiens

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<210> 8
<211> 339
<212> PRT
<213> Homo sapiens

<400> 8
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35 40 45
Lys Gly Val Asp Glu Val Thr Ile Val Asn Ile Leu Thr Asn Arg Ser
50 55 60
Asn Ala Gln Arg Gln Asp Ile Ala Phe Ala Tyr Gln Arg Arg Thr Lys
65 70 75 80
Lys Glu Leu Ala Ser Ala Leu Lys Ser Ala Leu Ser Gly His Leu Glu
85 90 95
Thr Val Ile Leu Gly Leu Leu Lys Thr Pro Ala Gln Tyr Asp Ala Ser
100 105 110
Glu Leu Lys Ala Ser Met Lys Gly Leu Gly Thr Asp Glu Asp Ser Leu
115 120 125
Ile Glu Ile Ile Cys Ser Arg Thr Asn Gln Glu Leu Gln Glu Ile Asn
130 135 140
Arg Val Tyr Lys Glu Met Tyr Lys Thr Asp Leu Glu Lys Asp Ile Ile
145 150 155 160
Ser Asp Thr Ser Gly Asp Phe Arg Lys Leu Met Val Ala Leu Ala Lys
165 170 175

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Gln Asp Ala Arg Asp Leu Tyr Asp Ala Gly Val Lys Arg Lys Gly Thr
        195                 200                 205
Asp Val Pro Lys Trp Ile Ser Ile Met Thr Glu Arg Ser Val Pro His
    210                 215                 220
Leu Gln Lys Val Phe Asp Arg Tyr Lys Ser Tyr Ser Pro Tyr Asp Met
225                 230                 235                 240
Leu Glu Ser Ile Arg Lys Glu Val Lys Gly Asp Leu Glu Asn Ala Phe
                245                 250                 255
Leu Asn Leu Val Gln Cys Ile Gln Asn Lys Pro Leu Tyr Phe Ala Asp
            260                 265                 270
Arg Leu Tyr Asp Ser Met Lys Gly Lys Gly Thr Arg Asp Lys Val Leu
        275                 280                 285
Ile Arg Ile Met Val Ser Arg Ser Glu Val Asp Met Leu Lys Ile Arg
    290                 295                 300
Ser Glu Phe Lys Arg Lys Tyr Gly Lys Ser Leu Tyr Tyr Tyr Ile Gln
305                 310                 315                 320
Gln Asp Thr Lys Gly Asp Tyr Gln Lys Ala Leu Leu Tyr Leu Cys Gly
                325                 330                 335
Gly Asp Asp
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<210> 9
<211> 1982
<212> DNA
<213> Homo sapiens

<400> 9

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caatgccatg gaagatgccc agaccctgag gaaggccatg aaagggctcg gcaccgatga 180
agacgccatt attagcgtcc ttgcctaccg caacaccgcc cagcgccagg agatcaggac 240
agcctacaag agcaccatcg gcagggactt gatagacgac ctgaagtcag aactgagtgg 300
caacttcgag caggtgattg tggggatgat gacgcccacg gtgctgtatg acgtgcaaga 360
gctgcgaagg gccatgaagg gagccggcac tgatgagggc tgcctaattg agatcctggc 420
ctcccggacc cctgaggaga tccggcgcat aagccaaacc taccagcagc aatatggacg 480
gagccttgaa gatgacattc gctctgacac atcgttcatg ttccagcgag tgctggtgtc 540
tctgtcagct ggtgggaggg atgaaggaaa ttatctggac gatgctctcg tgagacagga 600
tgcccaggac ctgtatgagg ctggagagaa gaaatggggg acagatgagg tgaaatttct 660
aactgttctc tgttcccgga accgaaatca cctgttgcat gtgtttgatg aatacaaaag 720
gatatcacag aaggatattg aacagagtat taaatctgaa acatctggta gctttgaaga 780
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tgtgtttcac agacattgaa tatattaaat tattccatat tttcttttca gtgaaaaatt 1380
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tatatttcat agtcaaagcc ttgaaagcat ctacaaatct cttttttag gttttgtcca 1560
tagcatcagt tgatccttac taagttttc atgggagact tccttcatca catcttatgt 1620
tgaaatcact ttctgtagtc aaagtatacc aaaaccaatt tatctgaact aaattctaaa 1680
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gtatggttat acaaaccata tacatctggt taccaaacat aaatgctgaa cattccatat 1740
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ctaggtattc tgggaatgat gtaatgctct gaatttagta tgatataaag aaaacttttt 1860
tgtgctaaaa atacttttta aaatcaattt tgttgattgt agtaatttct atttgcactg 1920
tgcctttcaa ctccagaaac attctaagat gtacttggat ttaattaaaa agttcacttt 1980
gt                                                                1982

<210> 10
<211> 321
<212> PRT
<213> Homo sapiens

<400> 10
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 1               5                  10                  15
Asn Ala Met Glu Asp Ala Gln Thr Leu Arg Lys Ala Met Lys Gly Leu
            20                  25                  30
Gly Thr Asp Glu Asp Ala Ile Ile Ser Val Leu Ala Tyr Arg Asn Thr
        35                  40                  45
Ala Gln Arg Gln Glu Ile Arg Thr Ala Tyr Lys Ser Thr Ile Gly Arg
    50                  55                  60
Asp Leu Ile Asp Asp Leu Lys Ser Glu Leu Ser Gly Asn Phe Glu Gln
65                  70                  75                  80
Val Ile Val Gly Met Met Thr Pro Thr Val Leu Tyr Asp Val Gln Glu
                85                  90                  95
Leu Arg Arg Ala Met Lys Gly Ala Gly Thr Asp Glu Gly Cys Leu Ile
            100                 105                 110
Glu Ile Leu Ala Ser Arg Thr Pro Glu Glu Ile Arg Arg Ile Ser Gln
        115                 120                 125
Thr Tyr Gln Gln Gln Tyr Gly Arg Ser Leu Glu Asp Asp Ile Arg Ser
    130                 135                 140
Asp Thr Ser Phe Met Phe Gln Arg Val Leu Val Ser Leu Ser Ala Gly
145                 150                 155                 160
Gly Arg Asp Glu Gly Asn Tyr Leu Asp Asp Ala Leu Val Arg Gln Asp
                165                 170                 175
Ala Gln Asp Leu Tyr Glu Ala Gly Glu Lys Lys Trp Gly Thr Asp Glu
            180                 185                 190
Val Lys Phe Leu Thr Val Leu Cys Ser Arg Asn Arg Asn His Leu Leu
        195                 200                 205
His Val Phe Asp Glu Tyr Lys Arg Ile Ser Gln Lys Asp Ile Glu Gln
    210                 215                 220
Ser Ile Lys Ser Glu Thr Ser Gly Ser Phe Glu Asp Ala Leu Leu Ala
225                 230                 235                 240
Ile Val Lys Cys Met Arg Asn Lys Ser Ala Tyr Phe Ala Glu Lys Leu
                245                 250                 255
Tyr Lys Ser Met Lys Gly Leu Gly Thr Asp Asp Asn Thr Leu Ile Arg
            260                 265                 270
Val Met Val Ser Arg Ala Glu Ile Asp Met Leu Asp Ile Arg Ala His
        275                 280                 285
Phe Lys Arg Leu Tyr Gly Lys Ser Leu Tyr Ser Phe Ile Lys Gly Asp
    290                 295                 300
Thr Ser Gly Asp Tyr Arg Lys Val Leu Leu Val Leu Cys Gly Gly Asp
305                 310                 315                 320
Asp


<210> 11
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<211> 1316
<212> DNA
<213> Homo sapiens

<400> 11
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cggggcgcac ggcaccgagg agagcgcggg agccaacctg ggcgcatcat gcgcagggcc 120
cgggacgctg ggccggtcta caccgccgcc tgggtcacgt ggcccggacg ggccggcggc 180
tgccccggcc ggggggcggg ggtcgcgccg gggttgcgct ggacgacgga gagcggcggg 240
cccgcagcgg cctggagcct cccaacccgc gccgcgctgg ccctcgagcg taggagccgc 300
cccctgcccc cccgcgccgg ccccgcgccc ggccgcccgc cccctatata gcgcgcccca 360
gcagggcccg cgccaggccg ccagcctcgg agtgggcgcg ggacagtgcg cggcgccccg 420
cagccaggcc cccgcccccg ccgcatccac ctcctccgcc gcctgcgacc caacgggcgc 480
cccccgccgg cagctcgcgc cgggcccccg cggccaccat gaagaaggag gtgtgctccg 540
tggccttcct caaggccgtg ttcgcagagt tcttggccac cctcatcttc gtcttctttg 600
gcctgggctc ggccctcaag tggccgtcgg cgctgcctac catcctgcag atcgcgctgg 660
cgtttggcct ggccataggc acgctggccc aggccctggg acccgtgagc ggcggccaca 720
tcaacccgc catcaccctg gccctcttgg tgggcaacca gatctcgctg ctccgggctt 780
tcttctacgt ggcggcccag ctggtgggcg ccattgccgg ggctggcatc ctctacggtg 840
tggcaccgct caatgcccgg ggcaatctgg ccgtcaacgc gctcaacaac aacacaacgc 900
agggccaggc catggtggtg gagctgattc tgaccttcca gctggcactc tgcatcttcg 960
cctccactga ctcccgccgc accagccctg tgggctcccc agccctgtcc attggcctgt 1020
ctgtcaccct gggccacctt gtcggaatct acttcactgg ctgctccatg aacccagccc 1080
gctcttttgg ccctgcggtg gtcatgaatc ggttcagccc cgctcactgg gtttctgggg 1140
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actccctgag cctgagtgag cgtgtggcca tcatcaaagg cacgtatgag cctgacgagg 1260
actgggagga gcagcgggaa gagcggaaga agaccatgga gctgaccacc cgctga 1316

<210> 12
<211> 265
<212> PRT
<213> Homo sapiens

<400> 12
Met Lys Lys Glu Val Cys Ser Val Ala Phe Leu Lys Ala Val Phe Ala
1 5 10 15
Glu Phe Leu Ala Thr Leu Ile Phe Val Phe Phe Gly Leu Gly Ser Ala
20 25 30
Leu Lys Trp Pro Ser Ala Leu Pro Thr Ile Leu Gln Ile Ala Leu Ala
35 40 45
Phe Gly Leu Ala Ile Gly Thr Leu Ala Gln Ala Leu Gly Pro Val Ser
50 55 60
Gly Gly His Ile Asn Pro Ala Ile Thr Leu Ala Leu Leu Val Gly Asn
65 70 75 80
Gln Ile Ser Leu Leu Arg Ala Phe Phe Tyr Val Ala Ala Gln Leu Val
85 90 95
Gly Ala Ile Ala Gly Ala Gly Ile Leu Tyr Gly Val Ala Pro Leu Asn
100 105 110
Ala Arg Gly Asn Leu Ala Val Asn Ala Leu Asn Asn Asn Thr Thr Gln
115 120 125
Gly Gln Ala Met Val Val Glu Leu Ile Leu Thr Phe Gln Leu Ala Leu
130 135 140
Cys Ile Phe Ala Ser Thr Asp Ser Arg Arg Thr Ser Pro Val Gly Ser
145 150 155 160
Pro Ala Leu Ser Ile Gly Leu Ser Val Thr Leu Gly His Leu Val Gly
165 170 175
Ile Tyr Phe Thr Gly Cys Ser Met Asn Pro Ala Arg Ser Phe Gly Pro
180 185 190

```
Ala Val Val Met Asn Arg Phe Ser Pro Ala His Trp Val Phe Trp Val
        195                 200                 205
Gly Pro Ile Val Gly Ala Val Leu Ala Ala Ile Leu Tyr Phe Tyr Leu
    210                 215                 220
Leu Phe Pro Asn Ser Leu Ser Leu Ser Glu Arg Val Ala Ile Ile Lys
225                 230                 235                 240
Gly Thr Tyr Glu Pro Asp Glu Asp Trp Glu Glu Gln Arg Glu Glu Arg
                245                 250                 255
Lys Lys Thr Met Glu Leu Thr Thr Arg
            260                 265
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<210> 13
<211> 1653
<212> DNA
<213> Homo. sapiens

<400> 13

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aagaggccct cggtggtgcc catggctggc caggatcctg cgctgagcac gagtcacccg 180
ttctacgacg tggccagaca tggcattctg caggtggcag gggatgaccg ctttggaaga 240
cgtgttgtca cgttcagctg ctgccggatg ccgccctccc acgagctgga ccaccagcgg 300
ctgctggagt atttgaagta cacactggac caatacgttg agaacgatta taccatcgtc 360
tatttccact acggctgaa cagccggaac aagccttccc tgggctggct ccagagcgca 420
tacaaggagt tcgataggaa agacggggat ctcactatgt ggcccaggct ggtctcgaac 480
tccaagctca agcgatcctc ccacctcagc ctcccaaagt actgggatta caggtacaag 540
aagaacttga aggccctcta cgtggtgcac ccccaccagct tcatcaaggt cctgtggaac 600
atcttgaagc ccctcatcag tcacaagttt gggaagaaag tcatctattt caactacctg 660
agtgagctcc acgaacacct taaatacgac cagctggtca tccctcccga agttttgcgg 720
tacgatgaga agctccagag cctgcacgag ggccggacgc cgcctcctac caagacacca 780
ccgccgcggc ccccgctgcc cacacagcag tttggcgtca gtctgcaata cctcaaagac 840
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aaaggcctgc gcaccgaggg cctgttccgg agatccgcca gcgtgcagac cgtccgcgag 960
atccagaggc tctacaacca agggaagccc gtgaactttg acgactacgg ggacattcac 1020
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cctttgcagg aggctgtgcc acggacacaa gccacgggcc tcaccaagcc taccctacct 1500
ccgagtcccc tgatggcagc cagaagacgt ctctagtgtt gcgaacactc tgtatgtttc 1560
gagctacctc ccacacctgt ctgtgcactt gtatgttttg taaacttggc atctgtaaaa 1620
ataaccagcc attagatgaa ttcagaacct tct                              1653
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<210> 14
<211> 464
<212> PRT
<213> Homo sapiens

<400> 14

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Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe.Tyr Asp
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Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
            20                  25                  30
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Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
        35                  40                  45
Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln
    50                  55                  60
Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn
65                  70                  75                  80
Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu
                85                  90                  95
Phe Asp Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser
            100                 105                 110
Asn Ser Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp
        115                 120                 125
Asp Tyr Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro
    130                 135                 140
Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser
145                 150                 155                 160
His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu
                165                 170                 175
His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu
            180                 185                 190
Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro
        195                 200                 205
Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe
    210                 215                 220
Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile
225                 230                 235                 240
Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu
                245                 250                 255
Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg
            260                 265                 270
Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp
        275                 280                 285
Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg
    290                 295                 300
Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu
305                 310                 315                 320
Gly Ile Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln
                325                 330                 335
Ile Leu Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu
            340                 345                 350
Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met
        355                 360                 365
Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro
    370                 375                 380
Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe
385                 390                 395                 400
Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu
                405                 410                 415
Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala
            420                 425                 430
Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr
        435                 440                 445
Lys Pro Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu
    450                 455                 460
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<210> 15
<211> 2043

<212> DNA
<213> Homo sapiens

<400> 15
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gccacctgga acagcatcca caacggggtg atcgccgtct tccagcgcaa ggggctgccc 180
gaccaggagc tcttcagcct caacgagggc gtccggcagc tgttgaagac agagctgggg 240
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gagccatcgg tgcgccagct ggccctgctg cacttccgga atgccatcac cctcagtgtg 480
aagctagagg atgcgctggc ccgggcccat gcccgtgtgc cccctgccat cgtgcagatg 540
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aagcccgtga actttgacga ctacggggac attcacatcc ctgccgtgat cctgaagacc 1440
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ccagagcaca actacgtcgt cctccgctac ctcatgggct tcctgcatgc ggtgtcccgg 1620
gagagcatct tcaacaaaat gaacagctct aacctggcct gtgtcttcgg gctgaatttg 1680
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gaactgctga tcgagtacta tgaaaagatc ttcagcaccc cggaggcacc tggggagcac 1800
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acacaagcca cgggcctcac caagcctacc ctacctccga gtcccctgat ggcagccaga 1920
agacgtctct agtgttgcga acactctgta tatttcgagc tacctcccac acctgtctgt 1980
gcacttgtat gttttgtaaa cttggcatct gtaaaaataa ccagccatta gatgaattca 2040
gaa 2043

<210> 16
<211> 643
<212> PRT
<213> Homo sapiens

<400> 16
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20 25 30
Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
35 40 45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50 55 60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65 70 75 80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85 90 95

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Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
            100                 105                 110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
        115                 120                 125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
    130                 135                 140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145                 150                 155                 160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
                165                 170                 175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
            180                 185                 190
Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
        195                 200                 205
Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe
    210                 215                 220
Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala
225                 230                 235                 240
Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala
                245                 250                 255
Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala
            260                 265                 270
Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg
        275                 280                 285
Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp
    290                 295                 300
His Gln Arg Leu Leu Glu Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val
305                 310                 315                 320
Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro
                325                 330                 335
Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu
            340                 345                 350
Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro
        355                 360                 365
Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg
    370                 375                 380
Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr
385                 390                 395                 400
Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly
                405                 410                 415
Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu
            420                 425                 430
Lys Gly Leu Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln
        435                 440                 445
Thr Val Arg Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn
    450                 455                 460
Phe Asp Asp Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr
465                 470                 475                 480
Phe Leu Arg Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu
                485                 490                 495
Gln Ile Leu Gly Ile Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly
            500                 505                 510
Cys Arg Gln Ile Leu Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu
        515                 520                 525
Arg Tyr Leu Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe
    530                 535                 540
Asn Lys Met Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu
545                 550                 555                 560
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Ile Trp Pro Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu
                565                 570                 575
Asn Met Phe Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser
            580                 585                 590
Thr Pro Glu Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly
        595                 600                 605
Ser Arg Ala Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr
    610                 615                 620
Gly Leu Thr Lys Pro Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg
625                 630                 635                 640
Arg Arg Leu
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<210> 17
<211> 2274
<212> DNA
<213> Homo sapiens

<400> 17

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gccacctgga acagcatcca caacggggtg atcgccgtct tccagcgcaa ggggctgccc 180
gaccaggagc tcttcagcct caacgagggc gtccggcagc tgttgaagac agagctgggg 240
tccttcttca cggagtacct gcagaaccag ctgctgacaa aaggcatggt gatccttcgg 300
gacaagattc gcttctatga gggacagaag ctgctggact cactggcaga gacctgggac 360
ttcttcttca gtgacgtgct gcccatgctg caggccatct tctacccggt gcagggcaag 420
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aagctagagg atgcgctggc ccgggcccat gcccgtgtgc cccctgccat cgtgcagatg 540
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cacgagctgg accaccagcg gctgctggag tatttgaagt acacactgga ccaatacgtt 960
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tgcgaacact ctgtatattt cgagctacct cccacacctg tctgtgcact tgtatgtttt 2220
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<210> 18
<211> 751
<212> PRT
<213> Homo sapiens

<220>
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<223> Xaa = Any Amino Acid

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20 25 30
Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
35 40 45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50 55 60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65 70 75 80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85 90 95
Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
100 105 110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
115 120 125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
130 135 140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145 150 155 160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
165 170 175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
180 185 190
Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
195 200 205
Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe
210 215 220
Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala
225 230 235 240
Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala
245 250 255
Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala
260 265 270
Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg
275 280 285
Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp
290 295 300
His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln Tyr Val
305 310 315 320
Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn Ser Arg
325 330 335
Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu Phe Asp
340 345 350
Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser Asn Ser
355 360 365

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Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr
    370                 375                 380
Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser
385                 390                 395                 400
Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys
                405                 410                 415
Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu
            420                 425                 430
His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr
        435                 440                 445
Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr
    450                 455                 460
Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val
465                 470                 475                 480
Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro Pro
                485                 490                 495
Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Arg Thr
            500                 505                 510
Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg Glu Ile
        515                 520                 525
Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp Tyr Gly
    530                 535                 540
Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg Glu Leu
545                 550                 555                 560
Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu Gly Ile
                565                 570                 575
Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln Ile Leu
            580                 585                 590
Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly
        595                 600                 605
Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser
    610                 615                 620
Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln
625                 630                 635                 640
Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu
                645                 650                 655
Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro
            660                 665                 670
Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro
        675                 680                 685
Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro
    690                 695                 700
Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu Xaa Cys
705                 710                 715                 720
Cys Glu His Ser Val Tyr Phe Glu Leu Pro Pro Thr Pro Val Cys Ala
                725                 730                 735
Leu Val Cys Phe Val Asn Leu Ala Ser Val Lys Ile Thr Ser His
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<210> 19
<211> 718
<212> PRT
<213> Homo sapiens

<400> 19

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Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
        35                  40                  45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
    50                  55                  60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65                  70                  75                  80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
                85                  90                  95
Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
            100                 105                 110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
        115                 120                 125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
    130                 135                 140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145                 150                 155                 160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
                165                 170                 175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
            180                 185                 190
Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
        195                 200                 205
Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe
    210                 215                 220
Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala
225                 230                 235                 240
Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala
                245                 250                 255
Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala
            260                 265                 270
Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg
        275                 280                 285
Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp
    290                 295                 300
His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln Tyr Val
305                 310                 315                 320
Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn Ser Arg
                325                 330                 335
Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu Phe Asp
            340                 345                 350
Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser Asn Ser
        355                 360                 365
Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr
    370                 375                 380
Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser
385                 390                 395                 400
Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys
                405                 410                 415
Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu
            420                 425                 430
His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr
        435                 440                 445
Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr
    450                 455                 460
Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val
465                 470                 475                 480
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Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro Pro
                485                 490                 495
Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Arg Thr
            500                 505                 510
Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val Arg Glu Ile
        515                 520                 525
Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe Asp Asp Tyr Gly
    530                 535                 540
Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr Phe Leu Arg Glu Leu
545                 550                 555                 560
Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr Glu Gln Ile Leu Gly Ile
                565                 570                 575
Thr Cys Val Glu Ser Ser Leu Arg Val Thr Gly Cys Arg Gln Ile Leu
            580                 585                 590
Arg Ser Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly
        595                 600                 605
Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser
    610                 615                 620
Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln
625                 630                 635                 640
Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu
                645                 650                 655
Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro
            660                 665                 670
Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro
        675                 680                 685
Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro
    690                 695                 700
Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu
705                 710                 715
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<210> 20
<211> 1431
<212> DNA
<213> Homo sapiens

<400> 20

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aagaggccct cggtggtgcc catggctggc caggatcctg cgctgagcac gagtcacccg 180
ttctacgacg tggccagaca tggcattctg caggtggcag gggatgaccg ctttggaaga 240
cgtgttgtca cgttcagctg ctgccggatg ccaccctccc acgagctgga ccaccagcgg 300
ctgctggaca ggtacaagaa gaacttgaag gccctctacg tggtgcaccc caccagcttc 360
atcaaggtcc tgtggaacat cttgaagccc ctcatcagtc acaagtttgg gaagaaagtc 420
atctatttca actacctgag tgagctccac gaacacctta aatacgacca gctggtcatc 480
cctcccgaag ttttgcggta cgatgagaag ctccagagcc tgcacgaggg ccggacgccg 540
cctcccacca agacaccacc gccgcggccc ccgctgccca cacagcagtt tggcgtcagt 600
ctgcaatacc tcaaagacaa aaatcaaggc gaactcatcc cccctgtgct gaggttcaca 660
gtgacgtacc tgagagagaa aggcctgcgc accgagggcc tgttccggag atccgccagc 720
gtgcagaccg tccgcgagat ccagaggctc tacaaccaag ggaagcccgt gaactttgac 780
gactacgggg acattcacat ccctgccgtg atcctgaaga ccttcctgcg agagctgccc 840
cagccgcttc tgaccttcca ggcctacgag cagattctcg ggatcacctg tgtggagagc 900
agcctgcgtg tcactggctg ccgccagatc ttacggagcc tcccagagca caactacgtc 960
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tatgaaaaga tcttcagcac cccggaggca cctggggagc acggcctggc accatgggaa 1200
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caggggagca gggcagcccc tttgcaggag gctgtgccac ggacacaagc cacgggcctc 1260
accaagccta ccctacctcc gagtcccctg atggcagcca gaagacgtct ctagtgttgc 1320
gaacactctg tatatttcga gctacctccc acacctgtct gtgcacttgt atgttttgta 1380
aacttggcat ctgtaaaaat aaccagccat tagatgaatt cagaaccttc t 1431

<210> 21
<211> 390
<212> PRT
<213> Homo sapiens

<400> 21
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Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
20 25 30
Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
35 40 45
Leu Asp His Gln Arg Leu Leu Asp Arg Tyr Lys Lys Asn Leu Lys Ala
50 55 60
Leu Tyr Val Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile
65 70 75 80
Leu Lys Pro Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe
85 90 95
Asn Tyr Leu Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val
100 105 110
Ile Pro Pro Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His
115 120 125
Glu Gly Arg Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro
130 135 140
Leu Pro Thr Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys
145 150 155 160
Asn Gln Gly Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr
165 170 175
Leu Arg Glu Lys Gly Leu Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala
180 185 190
Ser Val Gln Thr Val Arg Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys
195 200 205
Pro Val Asn Phe Asp Asp Tyr Gly Asp Ile His Ile Pro Ala Val Ile
210 215 220
Leu Lys Thr Phe Leu Arg Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln
225 230 235 240
Ala Tyr Glu Gln Ile Leu Gly Ile Thr Cys Val Glu Ser Ser Leu Arg
245 250 255
Val Thr Gly Cys Arg Gln Ile Leu Arg Ser Leu Pro Glu His Asn Tyr
260 265 270
Val Val Leu Arg Tyr Leu Met Gly Phe Leu His Ala Val Ser Arg Glu
275 280 285
Ser Ile Phe Asn Lys Met Asn Ser Ser Asn Leu Ala Cys Val Phe Gly
290 295 300
Leu Asn Leu Ile Trp Pro Ser Gln Gly Val Ser Ser Leu Ser Ala Leu
305 310 315 320
Val Pro Leu Asn Met Phe Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys
325 330 335
Ile Phe Ser Thr Pro Glu Ala Pro Gly Glu His Gly Leu Ala Pro Trp
340 345 350
Glu Gln Gly Ser Arg Ala Ala Pro Leu Gln Glu Ala Val Pro Arg Thr
355 360 365
Gln Ala Thr Gly Leu Thr Lys Pro Thr Leu Pro Pro Ser Pro Leu Met

370 375 380
Ala Ala Arg Arg Arg Leu
385 390

<210> 22
<211> 2019
<212> DNA
<213> Homo sapiens

<400> 22
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gccacctgga acagcatcca caacggggtg atcgccgtct tccagcgcaa ggggctgccc 180
gaccaggagc tcttcagcct caacgagggc gtccggcagc tgttgaagac agagctgggg 240
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gacaagattc gcttctatga gggacagaag ctgctggact cactggcaga gacctgggac 360
ttcttcttca gtgacgtgct gcccatgctg caggccatct tctacccggt gcagggcaag 420
gagccatcgg tgcgccagct ggccctgctg cacttccgga atgccatcac cctcagtgtg 480
aagctagagg atgcgctggc ccgggcccat gcccgtgtgc cccctgccat cgtgcagatg 540
ctgctggtgc tgcagggggt acatgagtcc aggggcgtga ctgaggacta cctgcgcctg 600
gagacgctgg tccagaaggt ggtgtcgcca tacctgggca cctacggcct ccactccagc 660
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gctgtgctgg gtgcagtgag gaagaggccc tcggtggtgc ccatggctgg ccaggatcct 780
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cacgagctgg accaccagcg gctgctggag tatttgaagt acacactgga ccaatacgtt 960
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tactgggatt acaggtacaa gaagaacttg aaggccctct acgtggtgca ccccaccagc 1200
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ccgcctccca ccaagacacc accgccgcgg cccccgctgc ccacacagca gtttggcgtc 1440
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acagtgacgt acctgagaga gaaaggcctc ccagagcaca actacgtcgt cctccgctac 1560
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agtgcccttg tgcccctgaa catgttcact gaactgctga tcgagtacta tgaaaagatc 1740
ttcagcaccc cggaggcacc tggggagcac ggcctggcac catgggaaca ggggagcagg 1800
gcagcccctt tgcaggaggc tgtgccacgg acacaagcca cggcctcac caagcctacc 1860
ctacctccga gtcccctgat ggcagccaga agacgtctct agtgttgcga acactctgta 1920
tatttcgagc tacctcccac acctgtctgt gcacttgtat gttttgtaaa cttggcatct 1980
gtaaaaataa ccagccatta gatgaattca gaaccttct 2019

<210> 23
<211> 633
<212> PRT
<213> Homo sapiens

<400> 23
Met Arg Thr Leu Arg Arg Leu Lys Phe Met Ser Ser Pro Ser Leu Ser
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Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
35 40 45

Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50 55 60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65 70 75 80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85 90 95
Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
100 105 110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
115 120 125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
130 135 140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145 150 155 160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
165 170 175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
180 185 190
Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
195 200 205
Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe
210 215 220
Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala
225 230 235 240
Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala
245 250 255
Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala
260 265 270
Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg
275 280 285
Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp
290 295 300
His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln Tyr Val
305 310 315 320
Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn Ser Arg
325 330 335
Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu Phe Asp
340 345 350
Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser Asn Ser
355 360 365
Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp Asp Tyr
370 375 380
Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro Thr Ser
385 390 395 400
Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys
405 410 415
Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu
420 425 430
His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr
435 440 445
Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr
450 455 460
Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val
465 470 475 480
Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro Pro
485 490 495
Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu Pro Glu
500 505 510

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His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly Phe Leu His Ala Val
        515                 520                 525
Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser Ser Asn Leu Ala Cys
    530                 535                 540
Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln Gly Val Ser Ser Leu
545                 550                 555                 560
Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu Leu Leu Ile Glu Tyr
                565                 570                 575
Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro Gly Glu His Gly Leu
            580                 585                 590
Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro Leu Gln Glu Ala Val
        595                 600                 605
Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro Thr Leu Pro Pro Ser
    610                 615                 620
Pro Leu Met Ala Ala Arg Arg Arg Leu
625                 630
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<210> 24
<211> 1398
<212> DNA
<213> Homo sapiens

<400> 24
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ctgctggagt atttgaagta cacactggac caatacgttg agaacgatta taccatcgtc 360
tatttccact acggcctgaa cagccggaac aagccttccc tgggctggct ccagagcgca 420
tacaaggagt tcgataggaa agacggggat ctcactatgt ggcccaggct ggtctcgaac 480
tccaagctca agcgatcctc ccacctcagc ctcccaaagt actgggatta caggtacaag 540
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<210> 25
<211> 379
<212> PRT
<213> Homo sapiens

<400> 25
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 1               5                  10                  15
Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
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                20                  25                  30
Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
        35                  40                  45
Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr Thr Leu Asp Gln
    50                  55                  60
Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe His Tyr Gly Leu Asn
65                  70                  75                  80
Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu Gln Ser Ala Tyr Lys Glu
                85                  90                  95
Phe Asp Arg Lys Asp Gly Asp Leu Thr Met Trp Pro Arg Leu Val Ser
            100                 105                 110
Asn Ser Lys Leu Lys Arg Ser Ser His Leu Ser Leu Pro Lys Tyr Trp
        115                 120                 125
Asp Tyr Arg Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val Val His Pro
    130                 135                 140
Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro Leu Ile Ser
145                 150                 155                 160
His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu
                165                 170                 175
His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu
            180                 185                 190
Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro
        195                 200                 205
Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe
    210                 215                 220
Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile
225                 230                 235                 240
Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu
                245                 250                 255
Pro Glu His Asn Tyr Val Val Leu Arg Tyr Leu Met Gly Phe Leu His
            260                 265                 270
Ala Val Ser Arg Glu Ser Ile Phe Asn Lys Met Asn Ser Ser Asn Leu
        275                 280                 285
Ala Cys Val Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln Gly Val Ser
    290                 295                 300
Ser Leu Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu Leu Leu Ile
305                 310                 315                 320
Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro Gly Glu His
                325                 330                 335
Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro Leu Gln Glu
            340                 345                 350
Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro Thr Leu Pro
        355                 360                 365
Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu
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<210> 26
<211> 1787
<212> DNA
<213> Homo sapiens

<400> 26
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tccttcttca cggagtacct gcagaaccag ctgctgacaa aaggcatggt gatccttcgg 300
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ttcttcttca gtgacgtgct gcccatgctg caggccatct tctacccggt gcagggcaag 420
gagccatcgg tgcgccagct ggccctgctg cacttccgga atgccatcac cctcagtgtg 480
aagctagagg atgcgctggc ccgggcccat gcccgtgtgc cccctgccat cgtgcagatg 540
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gctgtgctgg gtgcagtgag gaagaggccc tcggtggtgc ccatggctgg ccaggatcct 780
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gcgaacactc tgtatatttc gagctacctc ccacacctgt ctgtgcactt gtatgttttg 1740
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<210> 27
<211> 461
<212> PRT
<213> Homo sapiens

<400> 27
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Gln Gln Arg Arg Ala Cys Ala Asn Ala Thr Trp Asn Ser Ile His Asn
35 40 45
Gly Val Ile Ala Val Phe Gln Arg Lys Gly Leu Pro Asp Gln Glu Leu
50 55 60
Phe Ser Leu Asn Glu Gly Val Arg Gln Leu Leu Lys Thr Glu Leu Gly
65 70 75 80
Ser Phe Phe Thr Glu Tyr Leu Gln Asn Gln Leu Leu Thr Lys Gly Met
85 90 95
Val Ile Leu Arg Asp Lys Ile Arg Phe Tyr Glu Gly Gln Lys Leu Leu
100 105 110
Asp Ser Leu Ala Glu Thr Trp Asp Phe Phe Phe Ser Asp Val Leu Pro
115 120 125
Met Leu Gln Ala Ile Phe Tyr Pro Val Gln Gly Lys Glu Pro Ser Val
130 135 140
Arg Gln Leu Ala Leu Leu His Phe Arg Asn Ala Ile Thr Leu Ser Val
145 150 155 160
Lys Leu Glu Asp Ala Leu Ala Arg Ala His Ala Arg Val Pro Pro Ala
165 170 175
Ile Val Gln Met Leu Leu Val Leu Gln Gly Val His Glu Ser Arg Gly
180 185 190
Val Thr Glu Asp Tyr Leu Arg Leu Glu Thr Leu Val Gln Lys Val Val
195 200 205

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Ser Pro Tyr Leu Gly Thr Tyr Gly Leu His Ser Ser Glu Gly Pro Phe
    210                 215                 220
Thr His Ser Cys Ile Leu Glu Leu Gln Arg Asp Lys Ala Ala Ala Ala
225                 230                 235                 240
Ala Val Leu Gly Ala Val Arg Lys Arg Pro Ser Val Val Pro Met Ala
                245                 250                 255
Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr Asp Val Ala
            260                 265                 270
Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly Arg Arg
        275                 280                 285
Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu Leu Asp
    290                 295                 300
His Gln Arg Leu Leu Glu Tyr Lys Lys Asn Leu Lys Ala Leu Tyr Val
305                 310                 315                 320
Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile Leu Lys Pro
                325                 330                 335
Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe Asn Tyr Leu
            340                 345                 350
Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val Ile Pro Pro
        355                 360                 365
Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His Glu Gly Arg
    370                 375                 380
Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr
385                 390                 395                 400
Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly
                405                 410                 415
Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu
            420                 425                 430
Lys Ala Ser Gln Ser Thr Thr Thr Ser Ser Ser Ala Thr Ser Trp Ala
        435                 440                 445
Ser Cys Met Arg Cys Pro Gly Arg Ala Ser Ser Thr Lys
    450                 455                 460
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<210> 28
<211> 1176
<212> DNA
<213> Homo sapiens

<400> 28

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aagaggccct cggtggtgcc catggctggc caggatcctg cgctgagcac gagtcacccg 180
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cgtgttgtca cgttcagctg ctgccggatg ccaccctccc acgagctgga ccaccagcgg 300
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atcaaggtcc tgtggaacat cttgaagccc ctcatcagtc acaagtttgg gaagaaagtc 420
atctatttca actacctgag tgagctccac gaacacctta aatacgacca gctggtcatc 480
cctcccgaag ttttgcggta cgatgagaag ctccagagcc tgcacgaggg ccggacgccg 540
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gtgacgtacc tgagagagaa aggcctccca gagcacaact acgtcgtcct ccgctacctc 720
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gccccctttgc aggaggctgt gccacggaca caagccacgg gcctcaccaa gcctacccta 1020
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<210> 29
<211> 305
<212> PRT
<213> Homo sapiens

<400> 29
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Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg Phe Gly
20 25 30
Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro Ser His Glu
35 40 45
Leu Asp His Gln Arg Leu Leu Asp Arg Tyr Lys Lys Asn Leu Lys Ala
50 55 60
Leu Tyr Val Val His Pro Thr Ser Phe Ile Lys Val Leu Trp Asn Ile
65 70 75 80
Leu Lys Pro Leu Ile Ser His Lys Phe Gly Lys Lys Val Ile Tyr Phe
85 90 95
Asn Tyr Leu Ser Glu Leu His Glu His Leu Lys Tyr Asp Gln Leu Val
100 105 110
Ile Pro Pro Glu Val Leu Arg Tyr Asp Glu Lys Leu Gln Ser Leu His
115 120 125
Glu Gly Arg Thr Pro Pro Pro Thr Lys Thr Pro Pro Pro Arg Pro Pro
130 135 140
Leu Pro Thr Gln Gln Phe Gly Val Ser Leu Gln Tyr Leu Lys Asp Lys
145 150 155 160
Asn Gln Gly Glu Leu Ile Pro Pro Val Leu Arg Phe Thr Val Thr Tyr
165 170 175
Leu Arg Glu Lys Gly Leu Pro Glu His Asn Tyr Val Val Leu Arg Tyr
180 185 190
Leu Met Gly Phe Leu His Ala Val Ser Arg Glu Ser Ile Phe Asn Lys
195 200 205
Met Asn Ser Ser Asn Leu Ala Cys Val Phe Gly Leu Asn Leu Ile Trp
210 215 220
Pro Ser Gln Gly Val Ser Ser Leu Ser Ala Leu Val Pro Leu Asn Met
225 230 235 240
Phe Thr Glu Leu Leu Ile Glu Tyr Tyr Glu Lys Ile Phe Ser Thr Pro
245 250 255
Glu Ala Pro Gly Glu His Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg
260 265 270
Ala Ala Pro Leu Gln Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu
275 280 285
Thr Lys Pro Thr Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg
290 295 300
Leu
305

<210> 30
<211> 3257
<212> DNA
<213> Homo sapiens

<400> 30
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aagactgaga tagagaggct aaccaaggag ctcacggaga ccacccacga gaagatccag 180
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atgaaggatg aaatccgaga atataagttc cgggaggcac ggctccttca ggactatact 600
gaattggaag aagaaaatat cacattgcag aaactagtgt ccacgttgaa gcagaaccag 660
gttgaatacg aaggcttaaa gcatgagatt aagcgatttg aggaggagac ggtactgctg 720
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<210> 31
<211> 975
<212> PRT

<213> Homo sapiens

<400> 31

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Met Ala Ala Glu Glu Val Leu Gln Thr Val Asp His Tyr Lys Thr Glu
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Ile Glu Arg Leu Thr Lys Glu Leu Thr Glu Thr Thr His Glu Lys Ile
            20                  25                  30
Gln Ala Ala Glu Tyr Gly Leu Val Val Leu Glu Glu Lys Leu Thr Leu
        35                  40                  45
Lys Gln Gln Tyr Asp Glu Leu Glu Ala Glu Tyr Asp Ser Leu Lys Gln
    50                  55                  60
Glu Leu Glu Gln Leu Lys Glu Ala Phe Gly Gln Ser Phe Ser Ile His
65                  70                  75                  80
Arg Lys Val Ala Glu Asp Gly Glu Thr Arg Glu Glu Thr Leu Leu Gln
                85                  90                  95
Glu Ser Ala Ser Lys Glu Ala Tyr Tyr Leu Gly Lys Ile Leu Glu Met
            100                 105                 110
Gln Asn Glu Leu Lys Gln Ser Arg Ala Val Val Thr Asn Val Gln Ala
        115                 120                 125
Glu Asn Glu Arg Leu Thr Ala Val Val Gln Asp Leu Lys Glu Asn Asn
    130                 135                 140
Glu Met Val Glu Leu Gln Arg Ile Arg Met Lys Asp Glu Ile Arg Glu
145                 150                 155                 160
Tyr Lys Phe Arg Glu Ala Arg Leu Leu Gln Asp Tyr Thr Glu Leu Glu
                165                 170                 175
Glu Glu Asn Ile Thr Leu Gln Lys Leu Val Ser Thr Leu Lys Gln Asn
            180                 185                 190
Gln Val Glu Tyr Glu Gly Leu Lys His Glu Ile Lys Arg Phe Glu Glu
        195                 200                 205
Glu Thr Val Leu Leu Asn Ser Gln Leu Glu Asp Ala Ile Arg Leu Lys
    210                 215                 220
Glu Ile Ala Glu His Gln Leu Glu Glu Ala Leu Glu Thr Leu Lys Asn
225                 230                 235                 240
Glu Arg Glu Gln Lys Asn Asn Leu Arg Lys Glu Leu Ser Gln Tyr Ile
                245                 250                 255
Ser Leu Asn Asp Asn His Ile Ser Ile Ser Val Asp Gly Leu Lys Phe
            260                 265                 270
Ala Glu Asp Gly Ser Glu Pro Asn Asn Asp Asp Lys Met Asn Gly His
        275                 280                 285
Ile His Gly Pro Leu Val Lys Leu Asn Gly Asp Tyr Arg Thr Pro Thr
    290                 295                 300
Leu Arg Lys Gly Glu Ser Leu Asn Pro Val Ser Asp Leu Phe Ser Glu
305                 310                 315                 320
Leu Asn Ile Ser Glu Ile Gln Lys Leu Lys Gln Gln Leu Met Gln Val
                325                 330                 335
Glu Arg Glu Lys Ala Ile Leu Leu Ala Asn Leu Gln Glu Ser Gln Thr
            340                 345                 350
Gln Leu Glu His Thr Lys Gly Ala Leu Thr Glu Gln His Glu Arg Val
        355                 360                 365
His Arg Leu Thr Glu His Val Asn Ala Met Arg Gly Leu Gln Ser Ser
    370                 375                 380
Lys Glu Leu Lys Ala Glu Leu Asp Gly Glu Lys Gly Arg Asp Ser Gly
385                 390                 395                 400
Glu Glu Ala His Asp Tyr Glu Val Asp Ile Asn Gly Leu Glu Ile Leu
                405                 410                 415
Glu Cys Lys Tyr Arg Val Ala Val Thr Glu Val Ile Asp Leu Lys Ala
            420                 425                 430
Glu Ile Lys Ala Leu Lys Glu Lys Tyr Asn Lys Ser Val Glu Asn Tyr
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435 440 445
Thr Asp Glu Lys Ala Lys Tyr Glu Ser Lys Ile Gln Met Tyr Asp Glu
450 455 460
Gln Val Thr Ser Leu Glu Lys Thr Thr Lys Glu Ser Gly Glu Lys Met
465 470 475 480
Ala His Met Glu Lys Glu Leu Gln Lys Met Thr Ser Ile Ala Asn Glu
485 490 495
Asn His Ser Thr Leu Asn Thr Ala Gln Asp Glu Leu Val Thr Phe Ser
500 505 510
Glu Glu Leu Ala Gln Leu Tyr His His Val Cys Leu Cys Asn Asn Glu
515 520 525
Thr Pro Asn Arg Val Met Leu Asp Tyr Tyr Arg Gln Ser Arg Val Thr
530 535 540
Arg Ser Gly Ser Leu Lys Gly Pro Asp Asp Pro Arg Gly Leu Leu Ser
545 550 555 560
Pro Arg Leu Ala Arg Arg Gly Val Ser Ser Pro Val Glu Thr Arg Thr
565 570 575
Ser Ser Glu Pro Val Ala Lys Glu Ser Thr Glu Pro Ser Lys Glu Pro
580 585 590
Ser Pro Thr Lys Thr Pro Thr Ile Ser Pro Val Ile Thr Ala Pro Pro
595 600 605
Ser Ser Pro Val Leu Asp Thr Ser Asp Ile Arg Lys Glu Pro Met Asn
610 615 620
Ile Tyr Asn Leu Asn Ala Ile Ile Arg Asp Gln Ile Lys His Leu Gln
625 630 635 640
Lys Ala Val Asp Arg Ser Leu Gln Leu Ser Arg Gln Arg Ala Ala Ala
645 650 655
Arg Glu Leu Ala Pro Met Ile Asp Lys Asp Lys Glu Ala Leu Met Glu
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Ala Thr Leu Arg Ala Val Leu Lys Ala Asn Lys Gln Thr Ala Glu Val
690 695 700
Ala Leu Ala Asn Leu Lys Asn Lys Tyr Glu Asn Glu Lys Ala Met Val
705 710 715 720
Thr Glu Thr Met Thr Lys Leu Arg Asn Glu Leu Lys Ala Leu Lys Glu
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Asp Glu Tyr Val Thr Gln Leu Asp Glu Met Gln Arg Gln Leu Ala Ala
755 760 765
Ala Glu Asp Glu Lys Lys Thr Leu Asn Thr Leu Leu Arg Met Ala Ile
770 775 780
Gln Gln Lys Leu Ala Leu Thr Gln Arg Leu Glu Asp Leu Glu Phe Asp
785 790 795 800
His Glu Gln Ser Arg Arg Ser Lys Gly Lys Leu Gly Lys Ser Lys Ile
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Gly Ser Pro Lys Val Ser Gly Glu Ala Ser Val Thr Val Pro Thr Ile
820 825 830
Asp Thr Tyr Leu Leu His Ser Gln Gly Pro Gln Thr Pro Asn Ile Arg
835 840 845
Val Ser Ser Gly Thr Gln Arg Lys Arg Gln Phe Ser Pro Ser Leu Cys
850 855 860
Asp Gln Ser Arg Pro Arg Thr Ser Gly Ala Ser Tyr Leu Gln Asn Leu
865 870 875 880
Leu Arg Val Pro Pro Asp Pro Thr Ser Thr Glu Ser Phe Leu Leu Lys
885 890 895
Gly Pro Pro Ser Met Ser Glu Phe Ile Gln Gly His Arg Leu Ser Lys

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Glu Lys Arg Leu Thr Val Ala Pro Pro Asp Cys Gln Gln Pro Ala Ala
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Ser Val Pro Pro Gln Cys Ser Gln Leu Ala Gly Arg Gln Asp Cys Pro
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Thr Val Ser Pro Asp Thr Ala Leu Pro Glu Glu Gln Pro His Ser Ser
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Ser Gln Cys Ala Pro Leu His Cys Leu Ser Lys Pro Pro His Pro
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<210> 32
<211> 2717
<212> DNA
<213> Homo sapiens

<400> 32

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<212> PRT
<213> Homo sapiens

<400> 33
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Gln Arg Leu Lys Val Phe Ser Gly Ala Leu Gln Glu Ala Leu Thr Glu
His Tyr Lys His His Trp Phe Pro Glu Lys Pro Ser Lys Gly Ser Gly
Tyr Arg Cys Ile Arg Ile Asn His Lys Met Asp Pro Ile Ile Ser Arg
Val Ala Ser Gln Ile Gly Leu Ser Gln Pro Gln Leu His Gln Leu Leu
Pro Ser Glu Leu Thr Leu Trp Val Asp Pro Tyr Glu Val Ser Tyr Arg
Ile Gly Glu Asp Gly Ser Ile Cys Val Leu Tyr Glu Glu Ala Pro Leu
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<212> DNA
<213> Homo sapiens

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<210> 35
<211> 1390
<212> PRT
<213> Homo sapiens

<400> 35
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Ser Pro Gly Ala Thr Met Leu Asp Pro Ser Ser Ser Glu Glu Glu Ser
        35                  40                  45
Asp Glu Ile Val Glu Glu Glu Ser Gly Lys Glu Val Leu Gly Ser Ala
    50                  55                  60
Pro Ser Gly Ala Arg Leu Ser Pro Ser Arg Thr Ser Glu Gly Ser Ala
65                  70                  75                  80
Gly Ser Ala Gly Leu Gly Gly Gly Gly Ala Gly Ala Gly Ala Gly Val
                85                  90                  95
Gly Ala Gly Gly Gly Gly Gly Ser Gly Ala Ser Ser Gly Gly Gly Ala
            100                 105                 110
Gly Gly Leu Gln Pro Ser Ser Arg Ala Gly Gly Gly Arg Pro Ser Ser
        115                 120                 125
Pro Ser Pro Ser Val Val Ser Glu Lys Glu Lys Glu Glu Leu Glu Arg
    130                 135                 140
Leu Gln Lys Glu Glu Glu Glu Arg Lys Lys Arg Leu Gln Leu Tyr Val
145                 150                 155                 160
Phe Val Met Arg Cys Ile Ala Tyr Pro Phe Asn Ala Lys Gln Pro Thr
                165                 170                 175
Asp Met Ala Arg Arg Gln Gln Lys Ile Ser Lys Gln Gln Leu Gln Thr
            180                 185                 190
Val Lys Asp Arg Phe Gln Ala Phe Leu Asn Gly Glu Thr Gln Ile Met
        195                 200                 205
Ala Asp Glu Ala Phe Met Asn Ala Val Gln Ser Tyr Tyr Glu Val Phe
    210                 215                 220
Leu Lys Ser Asp Arg Val Ala Arg Met Val Gln Ser Gly Gly Cys Ser
225                 230                 235                 240
Ala Asn Asp Ser Arg Glu Val Phe Lys Lys His Ile Glu Lys Arg Val
                245                 250                 255
Arg Ser Leu Pro Glu Ile Asp Gly Leu Ser Lys Glu Thr Val Leu Ser
            260                 265                 270
Ser Trp Met Ala Lys Phe Asp Ala Ile Tyr Arg Gly Glu Glu Asp Pro
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Arg Lys Gln Gln Ala Arg Met Thr Ala Ser Ala Ala Ser Glu Leu Ile
        290                     295                     300
Leu Ser Lys Glu Gln Leu Tyr Glu Met Phe Gln Asn Ile Leu Gly Ile
305                     310                     315                     320
Lys Lys Phe Glu His Gln Leu Leu Tyr Asn Ala Cys Gln Leu Asp Asn
                325                     330                     335
Pro Asp Glu Gln Ala Ala Gln Ile Arg Arg Glu Leu Asp Gly Arg Leu
            340                     345                     350
Gln Met Ala Asp Gln Ile Ala Arg Glu Arg Lys Phe Pro Lys Phe Val
        355                     360                     365
Ser Lys Glu Met Glu Asn Met Tyr Ile Glu Glu Leu Lys Ser Ser Val
    370                     375                     380
Asn Leu Leu Met Ala Asn Leu Glu Ser Met Pro Val Ser Lys Gly Gly
385                     390                     395                     400
Glu Phe Lys Leu Gln Lys Leu Lys Arg Ser His Asn Ala Ser Ile Ile
                405                     410                     415
Asp Met Gly Glu Glu Ser Glu Asn Gln Leu Ser Lys Ser Asp Val Val
            420                     425                     430
Leu Ser Phe Ser Leu Glu Val Val Ile Met Glu Val Gln Gly Leu Lys
        435                     440                     445
Ser Leu Ala Pro Asn Arg Ile Val Tyr Cys Thr Met Glu Val Glu Gly
    450                     455                     460
Gly Glu Lys Leu Gln Thr Asp Gln Ala Glu Ala Ser Lys Pro Thr Trp
465                     470                     475                     480
Gly Thr Gln Gly Asp Phe Ser Thr Thr His Ala Leu Pro Ala Val Lys
                485                     490                     495
Val Lys Leu Phe Thr Glu Ser Thr Gly Val Leu Ala Leu Glu Asp Lys
            500                     505                     510
Glu Leu Gly Arg Val Ile Leu His Pro Thr Pro Asn Ser Pro Lys Gln
        515                     520                     525
Ser Glu Trp His Lys Met Thr Val Ser Lys Asn Cys Pro Asp Gln Asp
    530                     535                     540
Leu Lys Ile Lys Leu Ala Val Arg Met Asp Lys Pro Gln Asn Met Lys
545                     550                     555                     560
His Ser Gly Tyr Leu Trp Ala Ile Gly Lys Asn Val Trp Lys Arg Trp
                565                     570                     575
Lys Lys Arg Phe Phe Val Leu Val Gln Val Ser Gln Tyr Thr Phe Ala
            580                     585                     590
Met Cys Ser Tyr Arg Glu Lys Lys Ala Glu Pro Gln Glu Leu Leu Gln
        595                     600                     605
Leu Asp Gly Tyr Thr Val Asp Tyr Thr Asp Pro Gln Pro Gly Leu Glu
    610                     615                     620
Gly Gly Arg Ala Phe Phe Asn Ala Val Lys Glu Gly Asp Thr Val Ile
625                     630                     635                     640
Phe Ala Ser Asp Asp Glu Gln Asp Arg Ile Leu Trp Val Gln Ala Met
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Tyr Arg Ala Thr Gly Gln Ser His Lys Pro Val Pro Pro Thr Gln Val
            660                     665                     670
Gln Lys Leu Asn Ala Lys Gly Gly Asn Val Pro Gln Leu Asp Ala Pro
        675                     680                     685
Ile Ser Gln Phe Tyr Ala Asp Arg Ala Gln Lys His Gly Met Asp Glu
    690                     695                     700
Phe Ile Ser Ser Asn Pro Cys Asn Phe Asp His Ala Ser Leu Phe Glu
705                     710                     715                     720
Met Val Gln Arg Leu Thr Leu Asp His Arg Leu Asn Asp Ser Tyr Ser
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Cys Leu Gly Trp Phe Ser Pro Gly Gln Val Phe Val Leu Asp Glu Tyr
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    770                 775                 780
Leu Leu His Tyr Ser Phe Ala Phe Cys Ala Ser His Val His Gly Asn
785                 790                 795                 800
Arg Pro Asp Gly Ile Gly Thr Val Thr Val Glu Glu Lys Glu Arg Phe
                805                 810                 815
Glu Glu Ile Lys Glu Arg Leu Arg Val Leu Leu Glu Asn Gln Ile Thr
            820                 825                 830
His Phe Arg Tyr Cys Phe Pro Phe Gly Arg Pro Glu Gly Ala Leu Lys
        835                 840                 845
Ala Thr Leu Ser Leu Leu Glu Arg Val Leu Met Lys Asp Ile Val Thr
    850                 855                 860
Pro Val Pro Gln Glu Glu Val Lys Thr Val Ile Arg Lys Cys Leu Glu
865                 870                 875                 880
Gln Ala Ala Leu Val Asn Tyr Ser Arg Leu Ser Glu Tyr Ala Lys Ile
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Glu Glu Asn Gln Lys Asp Ala Glu Asn Val Gly Arg Leu Ile Thr Pro
            900                 905                 910
Ala Lys Lys Leu Glu Asp Thr Ile Arg Leu Ala Glu Leu Val Ile Glu
        915                 920                 925
Val Leu Gln Gln Asn Glu Glu His His Ala Glu Pro His Val Asp Lys
    930                 935                 940
Gly Glu Ala Phe Ala Trp Trp Ser Asp Leu Met Val Glu His Ala Glu
945                 950                 955                 960
Thr Phe Leu Ser Leu Phe Ala Val Asp Met Asp Ala Ala Leu Glu Val
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Gln Pro Pro Asp Thr Trp Asp Ser Phe Pro Leu Phe Gln Leu Leu Asn
            980                 985                 990
Asp Phe Leu Arg Thr Asp Tyr Asn Leu Cys Asn Gly Lys Phe His Lys
        995                 1000                1005
His Leu Gln Asp Leu Phe Ala Pro Leu Val Val Arg Tyr Val Asp Leu
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Met Glu Ser Ser Ile Ala Gln Ser Ile His Arg Gly Phe Glu Arg Glu
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Ser Trp Glu Pro Val Lys Ser Leu Thr Ser Asn Leu Pro Asn Val Asn
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Leu Pro Asn Val Asn Leu Pro Lys Val Pro Asn Leu Pro Val Asn Ile
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Pro Leu Gly Ile Pro Gln Met Pro Thr Phe Ser Ala Pro Ser Trp Met
        1075                1080                1085
Ala Ala Ile Tyr Asp Ala Asp Asn Gly Ser Gly Thr Ser Glu Asp Leu
    1090                1095                1100
Phe Trp Lys Leu Asp Ala Leu Gln Thr Phe Ile Arg Asp Leu His Trp
1105                1110                1115                1120
Pro Glu Glu Glu Phe Gly Lys His Leu Glu Gln Arg Leu Lys Leu Met
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Ala Ser Asp Met Ile Glu Ser Cys Val Lys Arg Thr Arg Ile Ala Phe
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Glu Val Lys Leu Gln Lys Thr Ser Arg Ser Thr Asp Phe Arg Val Pro
        1155                1160                1165
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<212> PRT

<213> Homo sapiens

<400> 37

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Gly Arg Val Leu Gly Arg Val Asn Phe Glu Asp Cys Thr Gly Arg Gln
    50                  55                  60
Arg Thr Ala Tyr Phe Ser Leu Asp Thr Arg Phe Lys Val Gly Thr Asp
65                  70                  75                  80
Gly Val Ile Thr Val Lys Arg Pro Leu Arg Phe His Asn Pro Gln Ile
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His Phe Leu Val Tyr Ala Trp Asp Ser Thr Tyr Arg Lys Phe Ser Thr
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Lys Val Thr Leu Asn Thr Val Gly His His His Arg Pro Pro Pro His
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Gln Ala Ser Val Ser Gly Ile Gln Ala Glu Leu Leu Thr Phe Pro Asn
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Ser Ser Pro Gly Leu Arg Arg Gln Lys Arg Asp Trp Val Ile Pro Pro
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Gln Ile Lys Ser Asn Lys Asp Lys Glu Gly Lys Val Phe Tyr Ser Ile
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Thr Gly Gln Gly Ala Asp Thr Pro Pro Val Gly Val Phe Ile Ile Glu
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Val Lys Glu Pro Leu Leu Pro Pro Glu Asp Asp Thr Arg Asp Asn Val
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Pro Ala Asn Pro Asp Glu Ile Gly Asn Phe Ile Asp Glu Asn Leu Lys
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Ala Ala Asp Thr Asp Pro Thr Ala Pro Pro Tyr Asp Ser Leu Leu Val
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<212> DNA
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<212> PRT
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130 135 140
Phe Ile Ile Lys Ile His Asp Ile Asn Asp Asn Glu Pro Ile Phe Thr
145 150 155 160
Lys Glu Val Tyr Thr Ala Thr Val Pro Glu Met Ser Asp Val Gly Thr
165 170 175
Phe Val Val Gln Val Thr Ala Thr Asp Ala Asp Asp Pro Thr Tyr Gly
180 185 190
Asn Ser Ala Lys Val Val Tyr Ser Ile Leu Gln Gly Gln Pro Tyr Phe
195 200 205

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Ser Val Glu Ser Glu Thr Gly Ile Ile Lys Thr Ala Leu Leu Asn Met
    210                 215                 220
Asp Arg Glu Asn Arg Glu Gln Tyr Gln Val Val Ile Gln Ala Lys Asp
225                 230                 235                 240
Met Gly Gly Gln Met Gly Gly Leu Ser Gly Thr Thr Thr Val Asn Ile
                245                 250                 255
Thr Leu Thr Asp Val Asn Asp Asn Pro Pro Arg Phe Pro Gln Ser Thr
            260                 265                 270
Tyr Gln Phe Lys Thr Pro Glu Ser Ser Pro Pro Gly Thr Pro Ile Gly
        275                 280                 285
Arg Ile Lys Ala Ser Asp Ala Asp Val Gly Glu Asn Ala Glu Ile Glu
    290                 295                 300
Tyr Ser Ile Thr Asp Gly Glu Gly Leu Asp Met Phe Asp Val Ile Thr
305                 310                 315                 320
Asp Gln Glu Thr Gln Glu Gly Ile Ile Thr Val Lys Lys Leu Leu Asp
                325                 330                 335
Phe Glu Lys Lys Lys Val Tyr Thr Leu Lys Val Glu Ala Ser Asn Pro
            340                 345                 350
Tyr Val Glu Pro Arg Phe Leu Tyr Leu Gly Pro Phe Lys Asp Ser Ala
        355                 360                 365
Thr Val Arg Ile Val Val Glu Asp Val Asp Glu Pro Pro Val Phe Ser
    370                 375                 380
Lys Leu Ala Tyr Ile Leu Gln Ile Arg Glu Asp Ala Gln Ile Asn Thr
385                 390                 395                 400
Thr Ile Gly Ser Val Thr Ala Gln Asp Pro Asp Ala Ala Arg Asn Pro
                405                 410                 415
Val Lys Tyr Ser Val Asp Arg His Thr Asp Met Asp Arg Ile Phe Asn
            420                 425                 430
Ile Asp Ser Gly Asn Gly Ser Ile Phe Thr Ser Lys Leu Leu Asp Arg
        435                 440                 445
Glu Thr Leu Leu Trp His Asn Ile Thr Val Ile Ala Thr Glu Ile Asn
    450                 455                 460
Asn Pro Lys Gln Ser Ser Arg Val Pro Leu Tyr Ile Lys Val Leu Asp
465                 470                 475                 480
Val Asn Asp Asn Ala Pro Glu Phe Ala Glu Phe Tyr Glu Thr Phe Val
                485                 490                 495
Cys Glu Lys Ala Lys Ala Asp Gln Leu Ile Gln Thr Leu His Ala Val
            500                 505                 510
Asp Lys Asp Asp Pro Tyr Ser Gly His Gln Phe Ser Phe Ser Leu Ala
        515                 520                 525
Pro Glu Ala Ala Ser Gly Ser Asn Phe Thr Ile Gln Asp Asn Lys Asp
    530                 535                 540
Asn Thr Ala Gly Ile Leu Thr Arg Lys Asn Gly Tyr Asn Arg His Glu
545                 550                 555                 560
Met Ser Thr Tyr Leu Leu Pro Val Val Ile Ser Asp Asn Asp Tyr Pro
                565                 570                 575
Val Gln Ser Ser Thr Gly Thr Val Thr Val Arg Val Cys Ala Cys Asp
            580                 585                 590
His His Gly Asn Met Gln Ser Cys His Ala Glu Ala Leu Ile His Pro
        595                 600                 605
Thr Gly Leu Ser Thr Gly Ala Leu Val Ala Ile Leu Leu Cys Ile Val
    610                 615                 620
Ile Leu Leu Val Thr Val Val Leu Phe Ala Ala Leu Arg Arg Gln Arg
625                 630                 635                 640
Lys Lys Glu Pro Leu Ile Ile Ser Lys Glu Asp Ile Arg Asp Asn Ile
                645                 650                 655
Val Ser Tyr Asn Asp Glu Gly Gly Gly Glu Glu Asp Thr Gln Ala Phe
            660                 665                 670
```

```
Asp Ile Gly Thr Leu Arg Asn Pro Glu Ala Ile Glu Asp Asn Lys Leu
        675                 680                 685
Arg Arg Asp Ile Val Pro Glu Ala Leu Phe Leu Pro Arg Arg Thr Pro
    690                 695                 700
Thr Ala Arg Asp Asn Thr Asp Val Arg Asp Phe Ile Asn Gln Arg Leu
705                 710                 715                 720
Lys Glu Asn Asp Thr Asp Pro Thr Ala Pro Pro Tyr Asp Ser Leu Ala
                725                 730                 735
Thr Tyr Ala Tyr Glu Gly Thr Gly Ser Val Ala Asp Ser Leu Ser Ser
            740                 745                 750
Leu Glu Ser Val Thr Thr Asp Ala Asp Gln Asp Tyr Asp Tyr Leu Ser
        755                 760                 765
Asp Trp Gly Pro Arg Phe Lys Lys Leu Ala Asp Met Tyr Gly Gly Val
    770                 775                 780
Asp Ser Asp Lys Asp Ser
785                 790
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<210> 40
<211> 987
<212> DNA
<213> Homo sapiens

<400> 40

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cggagagggg gagaacagac aacgggcggc ggggagcagc atggagccgg cggcggggag 60
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ggtgcgggcg ctgctggagg cgggggcgct gcccaacgca ccgaatagtt acggtcggag 180
gccgatccag gtcatgatga tgggcagcgc ccgagtggcg gagctgctgc tgctccacgg 240
cgcggagccc aactgcgccg accccgccac tctcacccga cccgtgcacg acgctgcccg 300
ggagggcttc ctggacacgc tggtggtgct gcaccgggcc ggggcgcggc tggacgtgcg 360
cgatgcctgg ggccgtctgc ccgtggacct ggctgaggag ctgggccatc gcgatgtcgc 420
acggtacctg cgcgcggctg cgggggggcac cagaggcagt aaccatgccc gcatagatgc 480
cgcggaaggt ccctcagaca tccccgattg aaagaaccag agaggctctg agaaacctcg 540
ggaaacttag atcatcagtc accgaaggtc ctacagggcc acaactgccc ccgccacaac 600
ccaccccgct ttcgtagttt tcatttagaa aatagagctt ttaaaaatgt cctgcctttt 660
aacgtagata taagccttcc cccactaccg taaatgtcca tttatatcat tttttatata 720
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cagcctccgg aagctgtcga cttcatgaca agcattttgt gaactaggga agctcagggg 900
ggttactggc ttctcttgag tcacactgct agcaaatggc agaaccaaag ctcaaataaa 960
aataaaataa ttttcattca ttcactc                                    987
```

<210> 41
<211> 156
<212> PRT
<213> Homo sapiens

<400> 41

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Met Glu Pro Ala Ala Gly Ser Ser Met Glu Pro Ser Ala Asp Trp Leu
1               5                   10                  15
Ala Thr Ala Ala Ala Arg Gly Arg Val Glu Glu Val Arg Ala Leu Leu
            20                  25                  30
Glu Ala Gly Ala Leu Pro Asn Ala Pro Asn Ser Tyr Gly Arg Arg Pro
        35                  40                  45
Ile Gln Val Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu
    50                  55                  60
Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr Arg
65                  70                  75                  80
```

```
Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val
                85                  90                  95
Leu His Arg Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly Arg
            100                 105                 110
Leu Pro Val Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala Arg
        115                 120                 125
Tyr Leu Arg Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala Arg
    130                 135                 140
Ile Asp Ala Ala Glu Gly Pro Ser Asp Ile Pro Asp
145                 150                 155


&lt;210&gt; 42
&lt;211&gt; 5142
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens

&lt;400&gt; 42
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cgagcccgag cccgagcccg agcccgagcc cgagcccgag cccgaacgca agcctgggag 120
cgcggagccc ggctagggac tcctcctatt tatggagcag gcacccaaca tggctgagcc 180
ccgggggccc gtagaccatg gagtccagat tcgcttcatc acagagccag tgagtggtgc 240
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cacaaatgac ttgtaatgtc gtgattaaaa aaattcctat attcttctgc aaatcaaacg 5040
ttctttccca atccaatcca gccttggttt tattttaaat taaatattaa aattacacat 5100
ttatattgaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa                    5142
```

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<210> 43
<211> 1203
<212> PRT
<213> Homo sapiens

<400> 43
Met Glu Gln Ala Pro Asn Met Ala Glu Pro Arg Gly Pro Val Asp His
 1               5                  10                  15
Gly Val Gln Ile Arg Phe Ile Thr Glu Pro Val Ser Gly Ala Glu Met
            20                  25                  30
Gly Thr Leu Arg Arg Gly Gly Arg Arg Pro Ala Lys Asp Ala Arg Ala
```

```
        35                  40                  45
Ser Thr Tyr Gly Val Ala Val Arg Val Gln Gly Ile Ala Gly Gln Pro
    50                  55                  60
Phe Val Val Leu Asn Ser Gly Glu Lys Gly Gly Asp Ser Phe Gly Val
65                  70                  75                  80
Gln Ile Lys Gly Ala Asn Asp Gln Gly Ala Ser Gly Ala Leu Ser Ser
                85                  90                  95
Asp Leu Glu Leu Pro Glu Asn Pro Tyr Ser Gln Val Lys Gly Phe Pro
            100                 105                 110
Ala Pro Ser Gln Ser Ser Thr Ser Asp Glu Glu Pro Gly Ala Tyr Trp
        115                 120                 125
Asn Gly Lys Leu Leu Arg Ser His Ser Gln Ala Ser Leu Ala Gly Pro
    130                 135                 140
Gly Pro Val Asp Pro Ser Asn Arg Ser Asn Ser Met Leu Glu Leu Ala
145                 150                 155                 160
Pro Lys Val Ala Ser Pro Gly Ser Thr Ile Asp Thr Ala Pro Leu Ser
                165                 170                 175
Ser Val Asp Ser Leu Ile Asn Lys Phe Asp Ser Gln Leu Gly Gly Gln
            180                 185                 190
Ala Arg Gly Arg Thr Gly Arg Arg Thr Arg Met Leu Pro Pro Glu Gln
        195                 200                 205
Arg Lys Arg Ser Lys Ser Leu Asp Ser Arg Leu Pro Arg Asp Thr Phe
    210                 215                 220
Glu Glu Arg Glu Arg Gln Ser Thr Asn His Trp Thr Ser Ser Thr Lys
225                 230                 235                 240
Tyr Asp Asn His Val Gly Thr Ser Lys Gln Pro Ala Gln Ser Gln Asn
                245                 250                 255
Leu Ser Pro Leu Ser Gly Phe Ser Arg Ser Arg Gln Thr Gln Asp Trp
            260                 265                 270
Val Leu Gln Ser Phe Glu Glu Pro Arg Arg Ser Ala Gln Asp Pro Thr
        275                 280                 285
Met Leu Gln Phe Lys Ser Thr Pro Asp Leu Leu Arg Asp Gln Gln Glu
    290                 295                 300
Ala Ala Pro Pro Gly Ser Val Asp His Met Lys Ala Thr Ile Tyr Gly
305                 310                 315                 320
Ile Leu Arg Glu Gly Ser Ser Glu Ser Glu Thr Ser Val Arg Arg Lys
                325                 330                 335
Val Ser Leu Val Leu Glu Lys Met Gln Pro Leu Val Met Val Ser Ser
            340                 345                 350
Gly Ser Thr Lys Ala Val Ala Gly Gln Gly Glu Leu Thr Arg Lys Val
        355                 360                 365
Glu Glu Leu Gln Arg Lys Leu Asp Glu Glu Val Lys Lys Arg Gln Lys
    370                 375                 380
Leu Glu Pro Ser Gln Val Gly Leu Glu Arg Gln Leu Glu Glu Lys Thr
385                 390                 395                 400
Glu Glu Cys Ser Arg Leu Gln Glu Leu Leu Glu Arg Arg Lys Gly Glu
                405                 410                 415
Ala Gln Gln Ser Asn Lys Glu Leu Gln Asn Met Lys Arg Leu Leu Asp
            420                 425                 430
Gln Gly Glu Asp Leu Arg His Gly Leu Glu Thr Gln Val Met Glu Leu
        435                 440                 445
Gln Asn Lys Leu Lys His Val Gln Gly Pro Glu Pro Ala Lys Glu Val
    450                 455                 460
Leu Leu Lys Asp Leu Leu Glu Thr Arg Glu Leu Leu Glu Glu Val Leu
465                 470                 475                 480
Glu Gly Lys Gln Arg Val Glu Glu Gln Leu Arg Leu Arg Glu Arg Glu
                485                 490                 495
Leu Thr Ala Leu Lys Gly Ala Leu Lys Glu Glu Val Ala Ser Arg Asp
```

```
            500                     505                     510
Gln Glu Val Glu His Val Arg Gln Gln Tyr Gln Arg Asp Thr Glu Gln
        515                     520                     525
Leu Arg Arg Ser Met Gln Asp Ala Thr Gln Asp His Ala Val Leu Glu
    530                     535                     540
Ala Glu Arg Gln Lys Met Ser Ala Leu Val Arg Gly Leu Gln Arg Glu
545                     550                     555                     560
Leu Glu Glu Thr Ser Glu Glu Thr Gly His Trp Gln Ser Met Phe Gln
                565                     570                     575
Lys Asn Lys Glu Asp Leu Arg Ala Thr Lys Gln Glu Leu Leu Gln Leu
            580                     585                     590
Arg Met Glu Lys Glu Glu Met Glu Glu Glu Leu Gly Glu Lys Ile Glu
        595                     600                     605
Val Leu Gln Arg Glu Leu Glu Gln Ala Arg Ala Ser Ala Gly Asp Thr
    610                     615                     620
Arg Gln Val Glu Val Leu Lys Lys Glu Leu Leu Arg Thr Gln Glu Glu
625                     630                     635                     640
Leu Lys Glu Leu Gln Ala Glu Arg Gln Ser Gln Glu Val Ala Gly Arg
                645                     650                     655
His Arg Asp Arg Glu Leu Glu Lys Gln Leu Ala Val Leu Arg Val Glu
            660                     665                     670
Ala Asp Arg Gly Arg Glu Leu Glu Glu Gln Asn Leu Gln Leu Gln Lys
        675                     680                     685
Thr Leu Gln Gln Leu Arg Gln Asp Cys Glu Glu Ala Ser Lys Ala Lys
    690                     695                     700
Met Val Ala Glu Ala Glu Ala Thr Val Leu Gly Gln Arg Arg Ala Ala
705                     710                     715                     720
Val Glu Thr Thr Leu Arg Glu Thr Gln Glu Glu Asn Asp Glu Phe Arg
                725                     730                     735
Arg Arg Ile Leu Gly Leu Glu Gln Gln Leu Lys Glu Thr Arg Gly Leu
            740                     745                     750
Val Asp Gly Gly Glu Ala Val Glu Ala Arg Leu Arg Asp Lys Leu Gln
        755                     760                     765
Arg Leu Glu Ala Glu Lys Gln Gln Leu Glu Glu Ala Leu Asn Ala Ser
    770                     775                     780
Gln Glu Glu Glu Gly Ser Leu Ala Ala Ala Lys Arg Ala Leu Glu Ala
785                     790                     795                     800
Arg Leu Glu Glu Ala Gln Arg Gly Leu Ala Arg Leu Gly Gln Glu Gln
                805                     810                     815
Gln Thr Leu Asn Arg Ala Leu Glu Glu Glu Gly Lys Gln Arg Glu Val
            820                     825                     830
Leu Arg Arg Gly Lys Ala Glu Leu Glu Glu Gln Lys Arg Leu Leu Asp
        835                     840                     845
Arg Thr Val Asp Arg Leu Asn Lys Glu Leu Glu Lys Ile Gly Glu Asp
    850                     855                     860
Ser Lys Gln Ala Leu Gln Gln Leu Gln Ala Gln Leu Glu Asp Tyr Lys
865                     870                     875                     880
Glu Lys Ala Arg Arg Glu Val Ala Asp Ala Gln Arg Gln Ala Lys Asp
                885                     890                     895
Trp Ala Ser Glu Ala Glu Lys Thr Ser Gly Gly Leu Ser Arg Leu Gln
            900                     905                     910
Asp Glu Ile Gln Arg Leu Arg Gln Ala Leu Gln Ala Ser Gln Ala Glu
        915                     920                     925
Arg Asp Thr Ala Arg Leu Asp Lys Glu Leu Leu Ala Gln Arg Leu Gln
    930                     935                     940
Gly Leu Glu Gln Glu Ala Glu Asn Lys Lys Arg Ser Gln Asp Asp Arg
945                     950                     955                     960
Ala Arg Gln Leu Lys Gly Leu Glu Glu Lys Val Ser Arg Leu Glu Thr
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965 970 975
Glu Leu Asp Glu Glu Lys Asn Thr Val Glu Leu Leu Thr Asp Arg Val
980 985 990
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Glu Arg Ser Ala Arg Gln Asp Leu Glu Cys Asp Lys Ile Ser Leu Glu
1010 1015 1020
Arg Gln Asn Lys Asp Leu Lys Thr Arg Leu Ala Ser Ser Glu Gly Phe
1025 1030 1035 1040
Gln Lys Pro Ser Ala Ser Leu Ser Gln Leu Glu Ser Gln Asn Gln Leu
1045 1050 1055
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1060 1065 1070
Ser Thr Asn Arg Lys Leu Glu Arg Lys Val Lys Glu Leu Ser Ile Gln
1075 1080 1085
Ile Glu Asp Glu Arg Gln His Val Asn Asp Gln Lys Asp Gln Leu Ser
1090 1095 1100
Leu Arg Val Lys Ala Leu Lys Arg Gln Val Asp Glu Ala Glu Glu Glu
1105 1110 1115 1120
Ile Glu Arg Leu Asp Gly Leu Arg Lys Lys Ala Gln Arg Glu Val Glu
1125 1130 1135
Glu Gln His Glu Val Asn Glu Gln Leu Gln Ala Arg Ile Lys Ser Leu
1140 1145 1150
Glu Lys Asp Ser Trp Arg Lys Ala Ser Arg Ser Ala Ala Glu Ser Ala
1155 1160 1165
Leu Lys Asn Glu Gly Leu Ser Ser Asp Glu Glu Phe Asp Ser Val Tyr
1170 1175 1180
Asp Pro Ser Ser Ile Ala Ser Leu Leu Thr Glu Ser Asn Leu Gln Thr
1185 1190 1195 1200
Ser Ser Cys

<210> 44
<211> 1925
<212> DNA
<213> Homo sapiens

<400> 44
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atctgtgact tcctccgcgg agccacagtc catagaaccc tcggccagca ggtcccctat 1080
gccaccaagg gcaaccagtg ggtaggatac gacgaccagg aaagcgtcaa aagcaaggtg 1140

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cagtacctga aggataggca gctggcaggc gccatggtat gggccctgga cctggatgac 1200
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gcactcgctg caacgtagcc ctctgttctg cacacagcac gggggccaag gatgccccgt 1320
ccccctctgg ctccagctgg ccgggagcct gatcacctgc cctgctgagt cccaggctga 1380
gcctcagtct ccctcccttg gggcctatgc agaggtccac aacacacaga tttgagctca 1440
gccctggtgg gcagagaggt agggatgggg ctgtggggat agtgaggcat cgcaatgtaa 1500
gactcgggat tagtacacac ttgttgatga ttaatggaaa tgtttacaga tccccaagcc 1560
tggcaaggga atttcttcaa ctccctgccc cctagccctc cttatcaaag gacaccattt 1620
tggcaagctc tatcaccaag gagccaaaca tcctacaaga cacagtgacc atactaatta 1680
taccccctgc aaagccagct tgaaaccttc acttaggaac gtaatcgtgt cccctatcct 1740
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cgctttgctt tggtctatct ttgagcgccc actagaccca ctggactcac ctccccccatc 1860
tcttctgggt tccttcctct gagccttggg acccctgagc ttgcagagat gaaggccgcc 1920
atgtt                                                             1925
```

<210> 45
<211> 383
<212> PRT
<213> Homo sapiens

<400> 45

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Met Gly Val Lys Ala Ser Gln Thr Gly Phe Val Val Leu Val Leu Leu
 1               5                  10                  15
Gln Cys Cys Ser Ala Tyr Lys Leu Val Cys Tyr Tyr Thr Ser Trp Ser
            20                  25                  30
Gln Tyr Arg Glu Gly Asp Gly Ser Cys Phe Pro Asp Ala Leu Asp Arg
        35                  40                  45
Phe Leu Cys Thr His Ile Ile Tyr Ser Phe Ala Asn Ile Ser Asn Asp
    50                  55                  60
His Ile Asp Thr Trp Glu Trp Asn Asp Val Thr Leu Tyr Gly Met Leu
65                  70                  75                  80
Asn Thr Leu Lys Asn Arg Asn Pro Asn Leu Lys Thr Leu Leu Ser Val
                85                  90                  95
Gly Gly Trp Asn Phe Gly Ser Gln Arg Phe Ser Lys Ile Ala Ser Asn
            100                 105                 110
Thr Gln Ser Arg Arg Thr Phe Ile Lys Ser Val Pro Pro Phe Leu Arg
        115                 120                 125
Thr His Gly Phe Asp Gly Leu Asp Leu Ala Trp Leu Tyr Pro Gly Arg
    130                 135                 140
Arg Asp Lys Gln His Phe Thr Thr Leu Ile Lys Glu Met Lys Ala Glu
145                 150                 155                 160
Phe Ile Lys Glu Ala Gln Pro Gly Lys Lys Gln Leu Leu Leu Ser Ala
                165                 170                 175
Ala Leu Ser Ala Gly Lys Val Thr Ile Asp Ser Ser Tyr Asp Ile Ala
            180                 185                 190
Lys Ile Ser Gln His Leu Asp Phe Ile Ser Ile Met Thr Tyr Asp Phe
        195                 200                 205
His Gly Ala Trp Arg Gly Thr Thr Gly His His Ser Pro Leu Phe Arg
    210                 215                 220
Gly Gln Glu Asp Ala Ser Pro Asp Arg Phe Ser Asn Thr Asp Tyr Ala
225                 230                 235                 240
Val Gly Tyr Met Leu Arg Leu Gly Ala Pro Ala Ser Lys Leu Val Met
                245                 250                 255
Gly Ile Pro Thr Phe Gly Arg Ser Phe Thr Leu Ala Ser Ser Glu Thr
            260                 265                 270
Gly Val Gly Ala Pro Ile Ser Gly Pro Gly Ile Pro Gly Arg Phe Thr
        275                 280                 285
Lys Glu Ala Gly Thr Leu Ala Tyr Tyr Glu Ile Cys Asp Phe Leu Arg
```

```
    290                 295                 300
Gly Ala Thr Val His Arg Thr Leu Gly Gln Gln Val Pro Tyr Ala Thr
305                 310                 315                 320
Lys Gly Asn Gln Trp Val Gly Tyr Asp Asp Gln Glu Ser Val Lys Ser
                325                 330                 335
Lys Val Gln Tyr Leu Lys Asp Arg Gln Leu Ala Gly Ala Met Val Trp
            340                 345                 350
Ala Leu Asp Leu Asp Asp Phe Gln Gly Ser Phe Cys Gly Gln Asp Leu
        355                 360                 365
Arg Phe Pro Leu Thr Asn Ala Ile Lys Asp Ala Leu Ala Ala Thr
    370                 375                 380
```

<210> 46
<211> 1528
<212> DNA
<213> Homo sapiens

<400> 46

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gcgccagcgc ctactccagg atcccgtagc cagacctcaa gccatggctg gtcccttctc 180
ccgtctgctg tccgcccgcc cgggactcag gctcctggct ttggccggag cggggtctct 240
agccgctggg tttctgctcc gaccggaacc tgtacgagct gccagtgaac gacggaggct 300
gtatcccccg agcgctgagt acccagacct ccgaaagcac aacaactgca tggccagtca 360
cctgacccca gcagtctatg cacggctctg cgacaagacc acacccactg gttggacgct 420
agatcagtgt atccagactg gcgtggacaa ccctggccac cccttcatca agactgtggg 480
catggtggct ggagatgagg agacctatga ggtatttgct gacctgtttg accctgtgat 540
ccaagagcga cacaatggat atgacccccg gacaatgaag cacaccacgg atctagatgc 600
cagtaaaatc cgttctggct actttgatga gaggtatgta ttgtcctcta gagtcagaac 660
tggccgaagc atccgaggac tcagtctgcc tccagcttgc actcgagcag agcgacgaga 720
ggtggaacgt gttgtggtgg atgcactgag tggcctgaag ggtgacctgg ctggacgtta 780
ctataggctc agtgagatga cagaggctga acagcagcag cttattgatg accactttct 840
gtttgataag cctgtgtccc cgttgctgac tgcagcagga atggctcgag actggccaga 900
tgctcgtgga atttggcaca acaatgagaa gagcttcctg atctgggtga atgaggagga 960
tcatacacgg gtgatctcca tggagaaggg tggtaacatg aagagagtgt ttgaaagatt 1020
ctgccgaggc ctcaaagagg tggagagact tatccaagaa cgtggctggg agttcatgtg 1080
gaatgagcgt ttgggataca tcttgacctg tccatctaac ctgggcactg gacttcgggc 1140
aggagtgcac atcaaactgc ccctgctaag caaagatagc cgcttcccaa agatcctgga 1200
gaacctaaga ctccaaaaac gtggtactgg aggagtggac actgctgcta caggcggtgt 1260
ctttgatatt tctaatttgg accgactagg caaatcagag gtggagctgg tgcaactggt 1320
catcgatgga gtaaactatt tgattgattg tgaacggcgt ctggagagag gccaggatat 1380
ccgcatcccc acacctgtca tccacaccaa gcattaactc cccatcgcca gctgatgact 1440
caagattccc aggagttttg ctcattctaa tgatggccca ttctacttgc tctggacctg 1500
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```

<210> 47
<211> 417
<212> PRT
<213> Homo sapiens

<400> 47

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Met Ala Gly Pro Phe Ser Arg Leu Leu Ser Ala Arg Pro Gly Leu Arg
1               5                   10                  15
Leu Leu Ala Leu Ala Gly Ala Gly Ser Leu Ala Ala Gly Phe Leu Leu
            20                  25                  30
Arg Pro Glu Pro Val Arg Ala Ala Ser Glu Arg Arg Arg Leu Tyr Pro
        35                  40                  45
```

```
Pro Ser Ala Glu Tyr Pro Asp Leu Arg Lys His Asn Asn Cys Met Ala
    50                  55                  60
Ser His Leu Thr Pro Ala Val Tyr Ala Arg Leu Cys Asp Lys Thr Thr
65                  70                  75                  80
Pro Thr Gly Trp Thr Leu Asp Gln Cys Ile Gln Thr Gly Val Asp Asn
                85                  90                  95
Pro Gly His Pro Phe Ile Lys Thr Val Gly Met Val Ala Gly Asp Glu
            100                 105                 110
Glu Thr Tyr Glu Val Phe Ala Asp Leu Phe Asp Pro Val Ile Gln Glu
        115                 120                 125
Arg His Asn Gly Tyr Asp Pro Arg Thr Met Lys His Thr Thr Asp Leu
    130                 135                 140
Asp Ala Ser Lys Ile Arg Ser Gly Tyr Phe Asp Glu Arg Tyr Val Leu
145                 150                 155                 160
Ser Ser Arg Val Arg Thr Gly Arg Ser Ile Arg Gly Leu Ser Leu Pro
                165                 170                 175
Pro Ala Cys Thr Arg Ala Glu Arg Arg Glu Val Glu Arg Val Val Val
            180                 185                 190
Asp Ala Leu Ser Gly Leu Lys Gly Asp Leu Ala Gly Arg Tyr Tyr Arg
        195                 200                 205
Leu Ser Glu Met Thr Glu Ala Glu Gln Gln Gln Leu Ile Asp Asp His
    210                 215                 220
Phe Leu Phe Asp Lys Pro Val Ser Pro Leu Leu Thr Ala Ala Gly Met
225                 230                 235                 240
Ala Arg Asp Trp Pro Asp Ala Arg Gly Ile Trp His Asn Asn Glu Lys
                245                 250                 255
Ser Phe Leu Ile Trp Val Asn Glu Glu Asp His Thr Arg Val Ile Ser
            260                 265                 270
Met Glu Lys Gly Gly Asn Met Lys Arg Val Phe Glu Arg Phe Cys Arg
        275                 280                 285
Gly Leu Lys Glu Val Glu Arg Leu Ile Gln Glu Arg Gly Trp Glu Phe
    290                 295                 300
Met Trp Asn Glu Arg Leu Gly Tyr Ile Leu Thr Cys Pro Ser Asn Leu
305                 310                 315                 320
Gly Thr Gly Leu Arg Ala Gly Val His Ile Lys Leu Pro Leu Leu Ser
                325                 330                 335
Lys Asp Ser Arg Phe Pro Lys Ile Leu Glu Asn Leu Arg Leu Gln Lys
            340                 345                 350
Arg Gly Thr Gly Gly Val Asp Thr Ala Ala Thr Gly Gly Val Phe Asp
        355                 360                 365
Ile Ser Asn Leu Asp Arg Leu Gly Lys Ser Glu Val Glu Leu Val Gln
    370                 375                 380
Leu Val Ile Asp Gly Val Asn Tyr Leu Ile Asp Cys Glu Arg Arg Leu
385                 390                 395                 400
Glu Arg Gly Gln Asp Ile Arg Ile Pro Thr Pro Val Ile His Thr Lys
                405                 410                 415
His
```

<210> 48
<211> 2365
<212> DNA
<213> Homo sapiens

<400> 48

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tcgccttcat ggtctccatc tcaggctggg tactggtgtc ctccacgctg cccaccgact 120
```

actggaaggt gtctaccatc gacggcacgg tcatcacaac cgccacctat tgggccaacc 180
tgtggaaggc gtgcgttacc gactccacgg gcgtctccaa ctgcaaggac ttcccctcca 240
tgctggcgct ggacggttat atacaggcat gtagaggact tatgatcgct gctgtcagcc 300
tgggcttctt tggttccata tttgcgctct ttggaatgaa gtgtaccaaa gtcggaggct 360
ccgataaagc caaagctaaa attgcttgtt tggctgggat tgtattcata ctgtcagggc 420
tgtgctcaat gactggatgt tccctatatg caaacaaaat cacaacggaa ttctttgatc 480
ctctctttgt tgagcaaaag tatgaattag gagccgctct gtttattgga tgggcaggag 540
cctcactgtg cataattggt ggtgtcatat tttgcttttc aatatctgac aacaacaaaa 600
cacccagata cacatacaac ggggccacat ctgtcatgtc ttctcggaca aagtatcatg 660
gtggagaaga ttttaaaaca acaaaccctt caaaacagtt tgataaaaat gcttatgtct 720
aaaagagctc gctggcaagc tgcctcttga gtttgttata aaagcgaact gttcacaaaa 780
tgatcccatc aaggccctcc cataattaac actcaaaact atttttaaaa tatgcatttg 840
aagcatctgt tgattgtatg gatgtaagtg ttcttacata gttagttata tactaatcat 900
tttctgttgt ggctttctat aaaaaataaa cagtttattt acaggatttg taaaatgttt 960
tctacattta tatagaacat gaaaagcatt tagtaccaaa ggttcaagaa gtattcgtac 1020
tctagccttt ttaatcattc atagatagaa gtctttgtac ccactcctta tgtttctttt 1080
cattcataaa caggtgtata aggaacaatg tcttataaac agcatggggg caatctgaga 1140
atattcctca aaaggtgtcc aggttaaata gacatgttac tggctgcaca caggcaaatt 1200
ctagtttgtt ttttttaagt attctacaac atttatttaa aaaggtaaat ctttttgttg 1260
aagcagcaag ttatctggta gaacttaact tctacaggat cagagaggat cttgctcatt 1320
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cattctcttt gatgtatgca gagagttacg tagcagggga tgttctctga tttattccac 1440
tggcaccatt agtgaatatt tagttgtttt cataaacgat gctgtgatga agactcatgt 1500
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catcgccaag gtgtgattgg aaaaattcaa aaaattgcaa cctcaggcat aaatgggtta 1860
aggacatccc aagcccaagt ggtacgtgcc tcactcagaa ctgacgggcc gagttctatc 1920
taggtgtgtc ttccagaacc tgtttacggc taactggata actgagagac ttgtcatttc 1980
taaagacatt taagttgctc cagggatttc tgaaaaaaga cacaggcttc ttcctagagc 2040
cagccctata taacatgccc acaagggcaa cagttatcac agttcataca cacctttcat 2100
gtcctgtctc actcactcct cacagccatc ctaggagata catattgttt tcatcctgca 2160
tttacagaaa aagaaatgaa aacagagagc ttaaataatt tgccacagta atgtcgaaac 2220
taggcctttg aaccaaggca gtctagggta aaatatagtt tcaaagtatg aataagaatt 2280
ggtatttgtg ttatctttga gtaagaaact gtccgatatg aatcacaacg tgggtgaatg 2340
tagtatttc ctgaagtgtg aaaga 2365

<210> 49
<211> 228
<212> PRT
<213> Homo sapiens

<400> 49
Met Ala Ser Thr Ala Ser Glu Ile Ile Ala Phe Met Val Ser Ile Ser
1 5 10 15
Gly Trp Val Leu Val Ser Ser Thr Leu Pro Thr Asp Tyr Trp Lys Val
20 25 30
Ser Thr Ile Asp Gly Thr Val Ile Thr Thr Ala Thr Tyr Trp Ala Asn
35 40 45
Leu Trp Lys Ala Cys Val Thr Asp Ser Thr Gly Val Ser Asn Cys Lys
50 55 60
Asp Phe Pro Ser Met Leu Ala Leu Asp Gly Tyr Ile Gln Ala Cys Arg
65 70 75 80
Gly Leu Met Ile Ala Ala Val Ser Leu Gly Phe Phe Gly Ser Ile Phe
85 90 95
Ala Leu Phe Gly Met Lys Cys Thr Lys Val Gly Gly Ser Asp Lys Ala

```
            100                     105                     110
Lys Ala Lys Ile Ala Cys Leu Ala Gly Ile Val Phe Ile Leu Ser Gly
        115                     120                     125
Leu Cys Ser Met Thr Gly Cys Ser Leu Tyr Ala Asn Lys Ile Thr Thr
    130                     135                     140
Glu Phe Phe Asp Pro Leu Phe Val Glu Gln Lys Tyr Glu Leu Gly Ala
145                     150                     155                     160
Ala Leu Phe Ile Gly Trp Ala Gly Ala Ser Leu Cys Ile Ile Gly Gly
                165                     170                     175
Val Ile Phe Cys Phe Ser Ile Ser Asp Asn Asn Lys Thr Pro Arg Tyr
            180                     185                     190
Thr Tyr Asn Gly Ala Thr Ser Val Met Ser Ser Arg Thr Lys Tyr His
        195                     200                     205
Gly Gly Glu Asp Phe Lys Thr Thr Asn Pro Ser Lys Gln Phe Asp Lys
    210                     215                     220
Asn Ala Tyr Val
225
```

<210> 50
<211> 1024
<212> DNA
<213> Homo sapiens

<400> 50

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gcaactcaag acacctgcag cagggcgtga gaaaaagtaa aagaccagta ttttcacatt 180
gccaggtacc agaaacacag aagactgaca cccgccactt aagtggggcc agggctggtg 240
tctgcccatg ttgccatcct gatgggctgc ttgccacaat gagggatctt cttcaataca 300
tcgcttgctt ctttgccttt ttctctgctg ggtttttgat tgtggccacc tggactgact 360
gttggatggt gaatgctgat gactctctgg aggtgagcac aaaatgccga ggcctctggt 420
gggaatgcgt cacaaatgct tttgatggga ttcgcacctg tgatgagtac gattccatac 480
ttgcggagca tcccttgaag ctggtggtaa ctcgagcgtt gatgattact gcagatattc 540
tagctgggtt tggatttctc accctgctcc ttggtcttga ctgcgtgaaa ttcctccctg 600
atgagccgta cattaaagtc cgcatctgct ttgttgctgg agccacgtta ctaatagcag 660
gtaccccagg aatcattggc tctgtgtggt atgctgttga tgtgtatgtg gaacgttcta 720
ctttggtttt gcacaatata tttcttggta tccaatataa atttggttgg tcctgttggc 780
tcggaatggc tgggtctctg ggttgctttt tggctggagc tgttctcacc tgctgcttat 840
atctttttaa agatgttgga cctgagagaa actatcctta ttccttgagg aaagcctatt 900
cagccgcggg tgtttccatg gccaagtcat actcagcccc tcgcacagag acggccaaaa 960
tgtatgctgt agacacaagg gtgtaaaatg cacgtttcag ggtgtgtttg catatgattt 1020
aatc                                                              1024
```

<210> 51
<211> 305
<212> PRT
<213> Homo sapiens

<400> 51

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Met Thr Ser Arg Thr Pro Leu Leu Val Thr Ala Cys Leu Tyr Tyr Ser
1               5                   10                  15
Tyr Cys Asn Ser Arg His Leu Gln Gln Gly Val Arg Lys Ser Lys Arg
            20                  25                  30
Pro Val Phe Ser His Cys Gln Val Pro Glu Thr Gln Lys Thr Asp Thr
        35                  40                  45
Arg His Leu Ser Gly Ala Arg Ala Gly Val Cys Pro Cys Cys His Pro
    50                  55                  60
```

```
Asp Gly Leu Leu Ala Thr Met Arg Asp Leu Leu Gln Tyr Ile Ala Cys
65                  70                  75                  80
Phe Phe Ala Phe Phe Ser Ala Gly Phe Leu Ile Val Ala Thr Trp Thr
                85                  90                  95
Asp Cys Trp Met Val Asn Ala Asp Asp Ser Leu Glu Val Ser Thr Lys
            100                 105                 110
Cys Arg Gly Leu Trp Trp Glu Cys Val Thr Asn Ala Phe Asp Gly Ile
        115                 120                 125
Arg Thr Cys Asp Glu Tyr Asp Ser Ile Leu Ala Glu His Pro Leu Lys
    130                 135                 140
Leu Val Val Thr Arg Ala Leu Met Ile Thr Ala Asp Ile Leu Ala Gly
145                 150                 155                 160
Phe Gly Phe Leu Thr Leu Leu Leu Gly Leu Asp Cys Val Lys Phe Leu
                165                 170                 175
Pro Asp Glu Pro Tyr Ile Lys Val Arg Ile Cys Phe Val Ala Gly Ala
            180                 185                 190
Thr Leu Leu Ile Ala Gly Thr Pro Gly Ile Ile Gly Ser Val Trp Tyr
        195                 200                 205
Ala Val Asp Val Tyr Val Glu Arg Ser Thr Leu Val Leu His Asn Ile
    210                 215                 220
Phe Leu Gly Ile Gln Tyr Lys Phe Gly Trp Ser Cys Trp Leu Gly Met
225                 230                 235                 240
Ala Gly Ser Leu Gly Cys Phe Leu Ala Gly Ala Val Leu Thr Cys Cys
                245                 250                 255
Leu Tyr Leu Phe Lys Asp Val Gly Pro Glu Arg Asn Tyr Pro Tyr Ser
            260                 265                 270
Leu Arg Lys Ala Tyr Ser Ala Ala Gly Val Ser Met Ala Lys Ser Tyr
        275                 280                 285
Ser Ala Pro Arg Thr Glu Thr Ala Lys Met Tyr Ala Val Asp Thr Arg
    290                 295                 300
Val
305
```

<210> 52
<211> 1665
<212> DNA
<213> Homo sapiens

<400> 52

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acggcccccа cagccggatc ccctcagcct tccaggtcct caactcccgt ggacgctgaa 180
caatggcctc catggggcta caggtaatgg gcatcgcgct ggccgtcctg ggctggctgg 240
ccgtcatgct gtgctgcgcg ctgcccatgt ggcgcgtgac ggccttcatc ggcagcaaca 300
ttgtcacctc gcagaccatc tgggagggcc tatggatgaa ctgcgtggtg cagagcaccg 360
gccagatgca gtgcaaggtg tacgactcgc tgctggcact gccgcaggac ctgcaggcgg 420
cccgcgccct cgtcatcatc agcatcatcg tggctgctct gggcgtgctg ctgtccgtgg 480
tgggggggcaa gtgtaccaac tgcctggagg atgaaagcgc caaggccaag accatgatcg 540
tggcgggcgt ggtgttcctg ttggccggcc ttatggtgat agtgccggtg tcctggacgg 600
cccacaacat catccaagac ttctacaatc cgctggtggc ctccgggcag aagcgggaga 660
tgggtgcctc gctctacgtc ggctgggccg cctccggcct gctgctcctt ggcggggggc 720
tgctttgctg caactgtcca ccccgcacag acaagcctta ctccgccaag tattctgctg 780
cccgctctgc tgctgccagc aactacgtgt aaggtgccac ggctccactc tgttcctctc 840
tgctttgttc ttccctggac tgagctcagc gcaggctgtg accccaggag ggccctgcca 900
cgggccactg gctgctgggg actggggact gggcagagac tgagccaggc aggaaggcag 960
cagccttcag cctctctggc ccactcggac aacttcccaa ggccgcctcc tgctagcaag 1020
aacagagtcc accctcctct ggatattggg gagggacgga agtgacaggg tgtggtggtg 1080
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gagtggggag ctggcttctg ctggccagga tagcttaacc ctgactttgg gatctgcctg 1140
catcggcgtt ggccactgtc cccatttaca ttttccccac tctgtctgcc tgcatctcct 1200
ctgttccggg taggccttga tatcacctct gggactgtgc cttgctcacc gaaacccgcg 1260
cccaggagta tggctgaggc cttgcccacc cacctgcctg ggaagtgcag agtggatgga 1320
cgggtttaga ggggaggggc gaaggtgctg taaacaggtt tgggcagtgg tgggggaggg 1380
ggccagagag gcggctcagg ttgcccagct ctgtggcctc aggactctct gcctcacccg 1440
cttcagccca gggcccctgg agactgatcc cctctgagtc ctctgcccct tccaaggaca 1500
ctaatgagcc tgggagggtg gcagggagga ggggacagct tcacccttgg aagtcctggg 1560
gtttttcctc ttccttcttt gtggtttctg ttttgtaatt taagaagagc tattcatcac 1620
tgtaattatt attattttct acaataaatg ggacctgtgc acagg 1665

<210> 53
<211> 209
<212> PRT
<213> Homo sapiens

<400> 53
Met Ala Ser Met Gly Leu Gln Val Met Gly Ile Ala Leu Ala Val Leu
1 5 10 15
Gly Trp Leu Ala Val Met Leu Cys Cys Ala Leu Pro Met Trp Arg Val
20 25 30
Thr Ala Phe Ile Gly Ser Asn Ile Val Thr Ser Gln Thr Ile Trp Glu
35 40 45
Gly Leu Trp Met Asn Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys
50 55 60
Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala
65 70 75 80
Arg Ala Leu Val Ile Ile Ser Ile Ile Val Ala Ala Leu Gly Val Leu
85 90 95
Leu Ser Val Val Gly Gly Lys Cys Thr Asn Cys Leu Glu Asp Glu Ser
100 105 110
Ala Lys Ala Lys Thr Met Ile Val Ala Gly Val Val Phe Leu Leu Ala
115 120 125
Gly Leu Met Val Ile Val Pro Val Ser Trp Thr Ala His Asn Ile Ile
130 135 140
Gln Asp Phe Tyr Asn Pro Leu Val Ala Ser Gly Gln Lys Arg Glu Met
145 150 155 160
Gly Ala Ser Leu Tyr Val Gly Trp Ala Ala Ser Gly Leu Leu Leu Leu
165 170 175
Gly Gly Gly Leu Leu Cys Cys Asn Cys Pro Pro Arg Thr Asp Lys Pro
180 185 190
Tyr Ser Ala Lys Tyr Ser Ala Ala Arg Ser Ala Ala Ala Ser Asn Tyr
195 200 205
Val

<210> 54
<211> 3457
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(3457)
<223> n = A,T,C or G

<400> 54

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gaaaagcatt attacattgg aattattgaa acgacttggg attatgcctc tgaccatggg 120
gaaaagaaac ttatttctgt tgacacggaa cattccaata tctatcttca aaatggccca 180
gatagaattg ggagactata taagaaggcc ctttatcttc agtacacaga tgaaaccttt 240
aggacaacta tagaaaaacc ggtctggctt gggtttttag gccctattat caaagctgaa 300
actggagata aagtttatgt acacttaaaa aaccttgcct ctaggcccta cacctttcat 360
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35 40 45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
50 55 60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
65 70 75 80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
85 90 95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
100 105 110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
115 120 125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
130 135 140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
145 150 155 160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
165 170 175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
180 185 190
Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys. Asp Ser Leu Asp Lys Glu
195 200 205
Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val
210 215 220
Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys
225 230 235 240
Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser
245 250 255
Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly
260 265 270
Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met
275 280 285
Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu
290 295 300
Thr Asn Lys Asn Tyr Arg Ile Asp Thr Ile Asn Leu Phe Pro Ala Thr
305 310 315 320
Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu
325 330 335
Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe
340 345 350
Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly
355 360 365
Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn
370 375 380
Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala
385 390 395 400
Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile

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Glu Thr Phe Thr Tyr Glu Trp Thr Val Pro Lys Glu Val Gly Pro Thr
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Lys Lys Gly Ser Leu His Ala Asn Gly Arg Gln Lys Asp Val Asp Lys
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Lys Glu Asp Glu Asp Phe Gln Glu Ser Asn Lys Met His Ser Met Asn
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Pro Asp Thr Glu Gly Thr Phe Asn Val Glu Cys Leu Thr Thr Asp His
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740 745 750
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915 920 925
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930 935 940
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala
945 950 955 960
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val
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980 985 990
Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg
995 1000 1005
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Thr Phe Gly Ser Leu Pro Gly Leu Ser Met Cys Ala Glu Asp Arg Val
    50                  55                  60
Lys Trp Tyr Leu Phe Gly Met Gly Asn Glu Val Asp Val His Ala Ala
65                  70                  75                  80
Phe Phe His Gly Gln Ala Leu Thr Asn Lys Asn Tyr Arg Ile Asp Thr
                85                  90                  95
Ile Asn Leu Phe Pro Ala Thr Leu Phe Asp Ala Tyr Met Val Ala Gln
            100                 105                 110
Asn Pro Gly Glu Trp Met Leu Ser Cys Gln Asn Leu Asn His Leu Lys
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Ala Gly Leu Gln Ala Phe Phe Gln Val Gln Glu Cys Asn Lys Ser Ser
    130                 135                 140
Ser Lys Asp Asn Ile Arg Gly Lys His Val Arg His Tyr Tyr Ile Ala
145                 150                 155                 160
Ala Glu Glu Ile Ile Trp Asn Tyr Ala Pro Ser Gly Ile Asp Ile Phe
                165                 170                 175
Thr Lys Glu Asn Leu Thr Ala Pro Gly Ser Asp Ser Ala Val Phe Phe
            180                 185                 190
Glu Gln Gly Thr Thr Arg Ile Gly Gly Ser Tyr Lys Lys Leu Val Tyr
        195                 200                 205
Arg Glu Tyr Thr Asp Ala Ser Phe Thr Asn Arg Lys Glu Arg Gly Pro
    210                 215                 220
Glu Glu Glu His Leu Gly Ile Leu Gly Pro Val Ile Trp Ala Glu Val
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Tyr Tyr Ser Pro Asn Tyr Asn Pro Gln Ser Arg Ser Val Pro Pro Ser
275 280 285
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Pro Lys Glu Val Gly Pro Thr Asn Ala Asp Pro Val Cys Leu Ala Lys
305 310 315 320
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325 330 335
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340 345 350
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355 360 365
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Thr Ala Pro Asp Gln Val Asp Lys Glu Asp Glu Asp Phe Gln Glu Ser
385 390 395 400
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420 425 430
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435 440 445
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450 455 460
Ser Leu Thr Leu His Met Trp Pro Asp Thr Glu Gly Thr Phe Asn Val
465 470 475 480
Glu Cys Leu Thr Thr Asp His Tyr Thr Gly Gly Met Lys Gln Lys Tyr
485 490 495
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Gly Glu Arg Thr Tyr Tyr Ile Ala Ala Val Glu Val Glu Trp Asp Tyr
515 520 525
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530 535 540
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545 550 555 560
Lys Tyr Lys Lys Val Val Tyr Arg Gln Tyr Thr Asp Ser Thr Phe Arg
565 570 575
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Pro Gln Leu His Ala Asp Val Gly Asp Lys Val Lys Ile Ile Phe Lys
595 600 605
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Glu Ser Ser Thr Val Thr Pro Thr Leu Pro Gly Glu Thr Leu Thr Tyr
625 630 635 640
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Cys Ile Pro Trp Ala Tyr Tyr Ser Thr Val Asp Gln Val Lys Asp Leu
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Tyr Ser Gly Leu Ile Gly Pro Leu Ile Val Cys Arg Arg Pro Tyr Leu
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Lys Val Phe Asn Pro Arg Arg Lys Leu Glu Phe Ala Leu Leu Phe Leu

690 695 700
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Tyr Ser Asp His Pro Glu Lys Val Asn Lys Asp Asp Glu Glu Phe Ile
725 730 735
Glu Ser Asn Lys Met His Ala Ile Asn Gly Arg Met Phe Gly Asn Leu
740 745 750
Gln Gly Leu Thr Met His Val Gly Asp Glu Val Asn Trp Tyr Leu Met
755 760 765
Gly Met Gly Asn Glu Ile Asp Leu His Thr Val His Phe His Gly His
770 775 780
Ser Phe Gln Tyr Lys His Arg Gly Val Tyr Ser Ser Asp Val Phe Asp
785 790 795 800
Ile Phe Pro Gly Thr Tyr Gln Thr Leu Glu Met Phe Pro Arg Thr Pro
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Gly Ile Trp Leu Leu His Cys His Val Thr Asp His Ile His Ala Gly
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<211> 3321
<212> DNA
<213> Homo sapiens

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<210> 59
<211> 1065
<212> PRT
<213> Homo sapiens

<400> 59

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Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
        35                  40                  45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
    50                  55                  60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
65                  70                  75                  80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
                85                  90                  95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
            100                 105                 110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
        115                 120                 125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
    130                 135                 140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
145                 150                 155                 160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
                165                 170                 175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
            180                 185                 190
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Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu
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Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val
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Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys
225                 230                 235                 240
Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser
                245                 250                 255
Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly
            260                 265                 270
Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met
        275                 280                 285
Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu
    290                 295                 300
Thr Asn Lys Asn Tyr Arg Ile Asp Thr Ile Asn Leu Phe Pro Ala Thr
305                 310                 315                 320
Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu
                325                 330                 335
Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe
            340                 345                 350
Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly
        355                 360                 365
Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn
    370                 375                 380
Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala
385                 390                 395                 400
Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile
                405                 410                 415
Gly Gly Ser Tyr Lys Lys Leu Val Tyr Arg Glu Tyr Thr Asp Ala Ser
            420                 425                 430
Phe Thr Asn Arg Lys Glu Arg Gly Pro Glu Glu Glu His Leu Gly Ile
        435                 440                 445
Leu Gly Pro Val Ile Trp Ala Glu Val Gly Asp Thr Ile Arg Val Thr
    450                 455                 460
Phe His Asn Lys Gly Ala Tyr Pro Leu Ser Ile Glu Pro Ile Gly Val
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Arg Phe Asn Lys Asn Asn Glu Gly Thr Tyr Tyr Ser Pro Asn Tyr Asn
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Pro Gln Ser Arg Ser Val Pro Pro Ser Ala Ser His Val Ala Pro Thr
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Pro Thr Lys Asp Ile Phe Thr Gly Leu Ile Gly Pro Met Lys Ile Cys
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Lys Lys Gly Ser Leu His Ala Asn Gly Arg Gln Lys Asp Val Asp Lys
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Glu Phe Tyr Leu Phe Pro Thr Val Phe Asp Glu Asn Glu Ser Leu Leu
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Leu Glu Asp Asn Ile Arg Met Phe Thr Thr Ala Pro Asp Gln Val Asp
        595                 600                 605
Lys Glu Asp Glu Asp Phe Gln Glu Ser Asn Lys Met His Ser Met Asn
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Gly Phe Met Tyr Gly Asn Gln Pro Gly Leu Thr Met Cys Lys Gly Asp
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Ser Val Val Trp Tyr Leu Phe Ser Ala Gly Asn Glu Ala Asp Val His
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Pro Asp Thr Glu Gly Thr Phe Asn Val Glu Cys Leu Thr Thr Asp His
    690                 695                 700
Tyr Thr Gly Gly Met Lys Gln Lys Tyr Thr Val Asn Gln Cys Arg Arg
705                 710                 715                 720
Gln Ser Glu Asp Ser Thr Phe Tyr Leu Gly Glu Arg Thr Tyr Tyr Ile
                725                 730                 735
Ala Ala Val Glu Val Glu Trp Asp Tyr Ser Pro Gln Arg Glu Trp Glu
            740                 745                 750
Lys Glu Leu His His Leu Gln Glu Gln Asn Val Ser Asn Ala Phe Leu
        755                 760                 765
Asp Lys Gly Glu Phe Tyr Ile Gly Ser Lys Tyr Lys Lys Val Val Tyr
    770                 775                 780
Arg Gln Tyr Thr Asp Ser Thr Phe Arg Val Pro Val Glu Arg Lys Ala
785                 790                 795                 800
Glu Glu Glu His Leu Gly Ile Leu Gly Pro Gln Leu His Ala Asp Val
                805                 810                 815
Gly Asp Lys Val Lys Ile Ile Phe Lys Asn Met Ala Thr Arg Pro Tyr
            820                 825                 830
Ser Ile His Ala His Gly Val Gln Thr Glu Ser Ser Thr Val Thr Pro
        835                 840                 845
Thr Leu Pro Gly Glu Thr Leu Thr Tyr Val Trp Lys Ile Pro Glu Arg
    850                 855                 860
Ser Gly Ala Gly Thr Glu Asp Ser Ala Cys Ile Pro Trp Ala Tyr Tyr
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Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro
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Leu Ile Val Cys Arg Arg Pro Tyr Leu Lys Val Phe Asn Pro Arg Arg
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Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser
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Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys
    930                 935                 940
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala
945                 950                 955                 960
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val
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Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp
            980                 985                 990
Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg
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Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln
    1010                1015                1020
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<212> DNA
<213> Homo sapiens

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<212> PRT
<213> Homo sapiens

<400> 61
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Trp Asp Tyr Ala Ser Asp His Gly Glu Lys Lys Leu Ile Ser Val Asp
35 40 45
Thr Glu His Ser Asn Ile Tyr Leu Gln Asn Gly Pro Asp Arg Ile Gly
50 55 60
Arg Leu Tyr Lys Lys Ala Leu Tyr Leu Gln Tyr Thr Asp Glu Thr Phe
65 70 75 80
Arg Thr Thr Ile Glu Lys Pro Val Trp Leu Gly Phe Leu Gly Pro Ile
85 90 95
Ile Lys Ala Glu Thr Gly Asp Lys Val Tyr Val His Leu Lys Asn Leu
100 105 110
Ala Ser Arg Pro Tyr Thr Phe His Ser His Gly Ile Thr Tyr Tyr Lys
115 120 125
Glu His Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Asp Phe Gln Arg
130 135 140
Ala Asp Asp Lys Val Tyr Pro Gly Glu Gln Tyr Thr Tyr Met Leu Leu
145 150 155 160
Ala Thr Glu Glu Gln Ser Pro Gly Glu Gly Asp Gly Asn Cys Val Thr
165 170 175
Arg Ile Tyr His Ser His Ile Asp Ala Pro Lys Asp Ile Ala Ser Gly
180 185 190
Leu Ile Gly Pro Leu Ile Ile Cys Lys Lys Asp Ser Leu Asp Lys Glu
195 200 205
Lys Glu Lys His Ile Asp Arg Glu Phe Val Val Met Phe Ser Val Val
210 215 220
Asp Glu Asn Phe Ser Trp Tyr Leu Glu Asp Asn Ile Lys Thr Tyr Cys
225 230 235 240
Ser Glu Pro Glu Lys Val Asp Lys Asp Asn Glu Asp Phe Gln Glu Ser
245 250 255
Asn Arg Met Tyr Ser Val Asn Gly Tyr Thr Phe Gly Ser Leu Pro Gly
260 265 270
Leu Ser Met Cys Ala Glu Asp Arg Val Lys Trp Tyr Leu Phe Gly Met
275 280 285
Gly Asn Glu Val Asp Val His Ala Ala Phe Phe His Gly Gln Ala Leu

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305                 310                 315                 320
Leu Phe Asp Ala Tyr Met Val Ala Gln Asn Pro Gly Glu Trp Met Leu
                325                 330                 335
Ser Cys Gln Asn Leu Asn His Leu Lys Ala Gly Leu Gln Ala Phe Phe
            340                 345                 350
Gln Val Gln Glu Cys Asn Lys Ser Ser Ser Lys Asp Asn Ile Arg Gly
        355                 360                 365
Lys His Val Arg His Tyr Tyr Ile Ala Ala Glu Glu Ile Ile Trp Asn
    370                 375                 380
Tyr Ala Pro Ser Gly Ile Asp Ile Phe Thr Lys Glu Asn Leu Thr Ala
385                 390                 395                 400
Pro Gly Ser Asp Ser Ala Val Phe Phe Glu Gln Gly Thr Thr Arg Ile
                405                 410                 415
Gly Gly Ser Tyr Lys Lys Leu Val Tyr Arg Glu Tyr Thr Asp Ala Ser
            420                 425                 430
Phe Thr Asn Arg Lys Glu Arg Gly Pro Glu Glu Glu His Leu Gly Ile
        435                 440                 445
Leu Gly Pro Val Ile Trp Ala Glu Val Gly Asp Thr Ile Arg Val Thr
    450                 455                 460
Phe His Asn Lys Gly Ala Tyr Pro Leu Ser Ile Glu Pro Ile Gly Val
465                 470                 475                 480
Arg Phe Asn Lys Asn Asn Glu Gly Thr Tyr Tyr Ser Pro Asn Tyr Asn
                485                 490                 495
Pro Gln Ser Arg Ser Val Pro Pro Ser Ala Ser His Val Ala Pro Thr
            500                 505                 510
Glu Thr Phe Thr Tyr Glu Trp Thr Val Pro Lys Glu Val Gly Pro Thr
        515                 520                 525
Asn Ala Asp Pro Val Cys Leu Ala Lys Met Tyr Tyr Ser Ala Val Asp
    530                 535                 540
Pro Thr Lys Asp Ile Phe Thr Gly Leu Ile Gly Pro Met Lys Ile Cys
545                 550                 555                 560
Lys Lys Gly Ser Leu His Ala Asn Gly Arg Gln Lys Asp Val Asp Lys
                565                 570                 575
Glu Phe Tyr Leu Phe Pro Thr Val Phe Asp Glu Asn Glu Ser Leu Leu
            580                 585                 590
Leu Glu Asp Asn Ile Arg Met Phe Thr Thr Ala Pro Asp Gln Val Asp
        595                 600                 605
Lys Glu Asp Glu Asp Phe Gln Glu Ser Asn Lys Met His Ser Met Asn
    610                 615                 620
Gly Phe Met Tyr Gly Asn Gln Pro Gly Leu Thr Met Cys Lys Gly Asp
625                 630                 635                 640
Ser Val Val Trp Tyr Leu Phe Ser Ala Gly Asn Glu Ala Asp Val His
                645                 650                 655
Gly Ile Tyr Phe Ser Gly Asn Thr Tyr Leu Trp Arg Gly Glu Arg Arg
            660                 665                 670
Asp Thr Ala Asn Leu Phe Pro Gln Thr Ser Leu Thr Leu His Met Trp
        675                 680                 685
Pro Asp Thr Glu Gly Thr Phe Asn Val Glu Cys Leu Thr Thr Asp His
    690                 695                 700
Tyr Thr Gly Gly Met Lys Gln Lys Tyr Thr Val Asn Gln Cys Arg Arg
705                 710                 715                 720
Gln Ser Glu Asp Ser Thr Phe Tyr Leu Gly Glu Arg Thr Tyr Tyr Ile
                725                 730                 735
Ala Ala Val Glu Val Glu Trp Asp Tyr Ser Pro Gln Arg Glu Trp Glu
            740                 745                 750
Lys Glu Leu His His Leu Gln Glu Gln Asn Val Ser Asn Ala Phe Leu
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            755                 760                 765
Asp Lys Gly Glu Phe Tyr Ile Gly Ser Lys Tyr Lys Lys Val Val Tyr
        770                 775                 780
Arg Gln Tyr Thr Asp Ser Thr Phe Arg Val Pro Val Glu Arg Lys Ala
785                 790                 795                 800
Glu Glu Glu His Leu Gly Ile Leu Gly Pro Gln Leu His Ala Asp Val
                805                 810                 815
Gly Asp Lys Val Lys Ile Ile Phe Lys Asn Met Ala Thr Arg Pro Tyr
            820                 825                 830
Ser Ile His Ala His Gly Val Gln Thr Glu Ser Ser Thr Val Thr Pro
        835                 840                 845
Thr Leu Pro Gly Glu Thr Leu Thr Tyr Val Trp Lys Ile Pro Glu Arg
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Ser Gly Ala Gly Thr Glu Asp Ser Ala Cys Ile Pro Trp Ala Tyr Tyr
865                 870                 875                 880
Ser Thr Val Asp Gln Val Lys Asp Leu Tyr Ser Gly Leu Ile Gly Pro
                885                 890                 895
Leu Ile Val Cys Arg Arg Pro Tyr Leu Lys Val Phe Asn Pro Arg Arg
            900                 905                 910
Lys Leu Glu Phe Ala Leu Leu Phe Leu Val Phe Asp Glu Asn Glu Ser
        915                 920                 925
Trp Tyr Leu Asp Asp Asn Ile Lys Thr Tyr Ser Asp His Pro Glu Lys
    930                 935                 940
Val Asn Lys Asp Asp Glu Glu Phe Ile Glu Ser Asn Lys Met His Ala
945                 950                 955                 960
Ile Asn Gly Arg Met Phe Gly Asn Leu Gln Gly Leu Thr Met His Val
                965                 970                 975
Gly Asp Glu Val Asn Trp Tyr Leu Met Gly Met Gly Asn Glu Ile Asp
            980                 985                 990
Leu His Thr Val His Phe His Gly His Ser Phe Gln Tyr Lys His Arg
        995                 1000                1005
Gly Val Tyr Ser Ser Asp Val Phe Asp Ile Phe Pro Gly Thr Tyr Gln
    1010                1015                1020
Thr Leu Glu Met Phe Pro Arg Thr Pro Gly Ile Trp Leu Leu His Cys
1025                1030                1035                1040
His Val Thr Asp His Ile His Ala Gly Met Glu Thr Thr Tyr Thr Val
                1045                1050                1055
Leu Gln Asn Glu Ala Ser Ser Glu Thr His Arg Arg Ile Trp Asn Val
            1060                1065                1070
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Lys Glu
    1090


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<211> 969
<212> DNA
<213> Homo sapiens

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<212> PRT
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35 40 45
Asp Thr Phe Tyr Ile Lys Thr Ser Thr Thr Val Arg Thr Thr Glu Ile
50 55 60
Asn Phe Lys Val Gly Glu Glu Phe Glu Glu Gln Thr Val Asp Gly Arg
65 70 75 80
Pro Cys Lys Ser Leu Val Lys Trp Glu Ser Glu Asn Lys Met Val Cys
85 90 95
Glu Gln Lys Leu Leu Lys Gly Glu Gly Pro Lys Thr Ser Trp Thr Arg
100 105 110
Glu Leu Thr Asn Asp Gly Glu Leu Ile Leu Thr Met Thr Ala Asp Asp
115 120 125
Val Val Cys Thr Arg Val Tyr Val Arg Glu
130 135

<210> 64
<211> 927
<212> DNA
<213> Homo sapiens

<400> 64
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aggctaggag ctgctgcagc catgtcggcc ctcagcctcc tcattctggg cctgctcacg 240
gcagtgccac ctgccagctg tcagcaaggc ctggggaacc ttcagccctg gatgcagggc 300
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<211> 114
<212> PRT
<213> Homo sapiens

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Gly Leu Ile Ala Val Ala Val Phe Leu Val Leu Val Ala Ile Ala Phe
35 40 45
Ala Val Asn His Phe Trp Cys Gln Glu Glu Pro Glu Pro Ala His Met
50 55 60
Ile Leu Thr Val Gly Asn Lys Ala Asp Gly Val Leu Val Gly Thr Asp
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Gly Arg Tyr Ser Ser Met Ala Ala Ser Phe Arg Ser Ser Glu His Glu
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Asn Ala Tyr Glu Asn Val Pro Glu Glu Glu Gly Lys Val Arg Ser Thr
100 105 110
Pro Met

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<211> 3641
<212> DNA
<213> Homo sapiens

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<210> 67
<211> 482
<212> PRT
<213> Homo sapiens

<400> 67

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Lys Arg Ser Met Lys Arg Asp Asp Thr Lys Asp Thr Tyr Lys Leu Pro
        35                  40                  45
His Arg Leu Ile Glu Lys Lys Arg Arg Asp Arg Ile Asn Glu Cys Ile
    50                  55                  60
Ala Gln Leu Lys Asp Leu Leu Pro Glu His Leu Lys Leu Thr Thr Leu
65                  70                  75                  80
Gly His Leu Glu Lys Ala Val Val Leu Glu Leu Thr Leu Lys His Leu
                85                  90                  95
Lys Ala Leu Thr Ala Leu Thr Glu Gln Gln His Gln Lys Ile Ile Ala
            100                 105                 110
Leu Gln Asn Gly Glu Arg Ser Leu Lys Ser Pro Ile Gln Ser Asp Leu
        115                 120                 125
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Asp Ala Phe His Ser Gly Phe Gln Thr Cys Ala Lys Glu Val Leu Gln
    130                 135                 140
Tyr Leu Ser Arg Phe Glu Ser Trp Thr Pro Arg Glu Pro Arg Cys Val
145                 150                 155                 160
Gln Leu Ile Asn His Leu His Ala Val Ala Thr Gln Phe Leu Pro Thr
                165                 170                 175
Pro Gln Leu Leu Thr Gln Gln Val Pro Leu Ser Lys Gly Thr Gly Ala
            180                 185                 190
Pro Ser Ala Ala Gly Ser Ala Ala Ala Pro Cys Leu Glu Arg Ala Gly
        195                 200                 205
Gln Lys Leu Glu Pro Leu Ala Tyr Cys Val Pro Val Ile Gln Arg Thr
    210                 215                 220
Gln Pro Ser Ala Glu Leu Ala Ala Glu Asn Asp Thr Asp Thr Asp Ser
225                 230                 235                 240
Gly Tyr Gly Gly Glu Ala Glu Ala Arg Pro Asp Arg Glu Lys Gly Lys
                245                 250                 255
Gly Ala Gly Ala Ser Arg Val Thr Ile Lys Gln Glu Pro Pro Gly Glu
            260                 265                 270
Asp Ser Pro Ala Pro Lys Arg Met Lys Leu Asp Ser Arg Gly Gly Gly
        275                 280                 285
Ser Gly Gly Gly Pro Gly Gly Gly Ala Ala Ala Ala Ala Ala Ala Leu
    290                 295                 300
Leu Gly Pro Asp Pro Ala Ala Ala Ala Ala Leu Leu Arg Pro Asp Ala
305                 310                 315                 320
Ala Leu Leu Ser Ser Leu Val Ala Phe Gly Gly Gly Gly Gly Ala Pro
                325                 330                 335
Phe Pro Gln Pro Ala Ala Ala Ala Ala Pro Phe Cys Leu Pro Phe Cys
            340                 345                 350
Phe Leu Ser Pro Ser Ala Ala Ala Ala Tyr Val Gln Pro Phe Leu Asp
        355                 360                 365
Lys Ser Gly Leu Glu Lys Tyr Leu Tyr Pro Ala Ala Ala Ala Ala Pro
    370                 375                 380
Phe Pro Leu Leu Tyr Pro Gly Ile Pro Ala Pro Ala Ala Ala Ala Ala
385                 390                 395                 400
Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Phe Pro Cys Leu Ser
                405                 410                 415
Ser Val Leu Ser Pro Pro Pro Glu Lys Ala Gly Ala Ala Ala Ala Thr
            420                 425                 430
Leu Leu Pro His Glu Val Ala Pro Leu Gly Ala Pro His Pro Gln His
        435                 440                 445
Pro His Gly Arg Thr His Leu Pro Phe Ala Gly Pro Arg Glu Pro Gly
    450                 455                 460
Asn Pro Glu Ser Ser Ala Gln Glu Asp Pro Ser Gln Pro Gly Lys Glu
465                 470                 475                 480
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<210> 68
<211> 3624
<212> DNA
<213> Homo sapiens

<400> 68

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<210> 69
<211> 341
<212> PRT
<213> Homo sapiens

<400> 69
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35 40 45
Gly Arg Leu Phe Ala Leu Glu Phe Ala Arg Arg Arg Ala Leu Leu Val
50 55 60
Leu Trp Asp Ile Asn Thr Gln Ser Asn Glu Glu Thr Ala Gly Met Val
65 70 75 80
Arg His Ile Tyr Arg Asp Leu Glu Ala Ala Asp Ala Ala Ala Leu Gln
85 90 95
Ala Gly Asn Gly Glu Glu Glu Ile Leu Pro His Cys Asn Leu Gln Val
100 105 110
Phe Thr Tyr Thr Cys Asp Val Gly Lys Arg Glu Asn Val Tyr Leu Thr
115 120 125
Ala Glu Arg Val Arg Lys Glu Val Gly Glu Val Ser Val Leu Val Asn
130 135 140
Asn Ala Gly Val Val Ser Gly His His Leu Leu Glu Cys Pro Asp Glu
145 150 155 160
Leu Ile Glu Arg Thr Met Met Val Asn Cys His Ala His Phe Trp Thr
165 170 175
Thr Lys Ala Phe Leu Pro Thr Met Leu Glu Ile Asn His Gly His Ile
180 185 190
Val Thr Val Ala Ser Ser Leu Gly Leu Phe Ser Thr Ala Gly Val Glu
195 200 205
Asp Tyr Cys Ala Ser Lys Phe Gly Val Val Gly Phe His Glu Ser Leu
210 215 220
Ser His Glu Leu Lys Ala Ala Glu Lys Asp Gly Ile Lys Thr Thr Leu
225 230 235 240
Val Cys Pro Tyr Leu Val Asp Thr Gly Met Phe Arg Gly Cys Arg Ile
245 250 255
Arg Lys Glu Ile Glu Pro Phe Leu Pro Pro Leu Lys Pro Asp Tyr Cys
260 265 270
Val Lys Gln Ala Met Lys Ala Ile Leu Thr Asp Gln Pro Met Ile Cys
275 280 285
Thr Pro Arg Leu Met Tyr Ile Val Thr Phe Met Lys Ser Ile Leu Pro
290 295 300
Phe Glu Ala Val Val Cys Met Tyr Arg Phe Leu Gly Ala Asp Lys Cys
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Ala Lys Asn Gly Ile
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<210> 70
<211> 1428
<212> DNA
<213> Homo sapiens

<400> 70

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<210> 71
<211> 289
<212> PRT
<213> Homo sapiens

<400> 71

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            20                  25                  30
Glu Ser Pro Thr Leu Pro Glu Ser Ser Ala Thr Asp Ser Asp Tyr Tyr
        35                  40                  45
Ser Pro Thr Gly Gly Ala Pro His Gly Tyr Cys Ser Pro Thr Ser Ala
    50                  55                  60
Ser Tyr Gly Lys Ala Leu Asn Pro Tyr Gln Tyr Gln Tyr His Gly Val
65                  70                  75                  80
Asn Gly Ser Ala Gly Ser Tyr Pro Ala Lys Ala Tyr Ala Asp Tyr Ser
                85                  90                  95
Tyr Ala Ser Ser Tyr His Gln Tyr Gly Gly Ala Tyr Asn Arg Val Pro
            100                 105                 110
Ser Ala Thr Asn Gln Pro Glu Lys Glu Val Thr Glu Pro Glu Val Arg
        115                 120                 125
Met Val Asn Gly Lys Pro Lys Lys Val Arg Lys Pro Arg Thr Ile Tyr
    130                 135                 140
Ser Ser Phe Gln Leu Ala Ala Leu Gln Arg Arg Phe Gln Lys Thr Gln
145                 150                 155                 160
Tyr Leu Ala Leu Pro Glu Arg Ala Glu Leu Ala Ala Ser Leu Gly Leu
                165                 170                 175
Thr Gln Thr Gln Val Lys Ile Trp Phe Gln Asn Lys Arg Ser Lys Ile
            180                 185                 190
Lys Lys Ile Met Lys Asn Gly Glu Met Pro Pro Glu His Ser Pro Ser
        195                 200                 205
Ser Ser Asp Pro Met Ala Cys Asn Ser Pro Gln Ser Pro Ala Val Trp
```

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    210                 215                 220
Glu Pro Gln Gly Ser Ser Arg Ser Leu Ser His His Pro His Ala His
225                 230                 235                 240
Pro Pro Thr Ser Asn Gln Ser Pro Ala Ser Ser Tyr Leu Glu Asn Ser
                245                 250                 255
Ala Ser Trp Tyr Thr Ser Ala Ala Ser Ser Ile Asn Ser His Leu Pro
            260                 265                 270
Pro Pro Gly Ser Leu Gln His Pro Leu Ala Leu Ala Ser Gly Thr Leu
        275                 280                 285
Tyr
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<210> 72
<211> 2036
<212> DNA
<213> Homo sapiens

<400> 72
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caaggaggaa atggactggg caacgcagcc ggtttcggga gtgtgcacca ggactatcct 180
tcctaccccg gcttccccca gagccagtac ccccagtatt acggctcatc ctacaaccct 240
ccctacgtcc cggccagcag catctgccct tcgcccctct ccacgtccac ctacgtcctc 300
caggaggcat ctcacaacgt ccccaaccag agttccgagt cacttgctgg tgaatacaac 360
acacacaatg gaccttccac accagcgaaa gagggagaca cagacaggcc gcaccgggcc 420
tccgacggga agctccgagg ccggtctaag aggagcagtg acccgtcccc ggcaggggac 480
aatgagattg agcgtgtgtt cgtgtgggac ttggatgaga caataattat ttttcactcc 540
ttactcacgg ggacatttgc atccagatac gggaaggaca ccacgacgtc cgtgcgcatt 600
ggccttatga tggaagagat gatcttcaac cttgcagata cacatctgtt cttcaatgac 660
ctggaggatt gtgaccagat ccacgttgat gacgtctcat cagatgacaa tggccaagat 720
ttaagcacat acaacttctc cgctgacggc ttccacagtt cggccccagg agccaacctg 780
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gagaggataa tgcagagatt cggcagaaaa gctgtctacg tggtgatcgg tgatggtgtg 1200
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accatctcag aagccgtcca tcagtccaaa tgggggttct gagaaggaaa gtacccaaca 1500
ttggcttcgg agtatttgac tttggggaaa agggctggct cggagtctag actcttctgt 1560
aagactcaca gaacaaaagc aaggaattgc caatttgggg ggtgcctggt gatgaggagg 1620
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gctcttgtac ctgtgtggct gggtttctta gtcgttggtt tggtttggtt ttttgaactg 1740
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gcttattttt gtttttaaag acctacttga cgtcatgtgg acagtgcacg tgccttacgc 1920
tacatcttgt tttctaggaa gagggggatg ctgggaagga atgggtgctt tgtgatggat 1980
aaaaggcatt aaataaaacc acgtttacat tttgaaaaaa aaaaaaaaaa aaaaaa     2036

<210> 73
<211> 434
<212> PRT
<213> Homo sapiens
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<400> 73
Asp Ser Leu Asn His Ser Pro Gly Gln Ser Gly Phe Leu Ser Tyr Gly
 1               5                   10                  15
Ser Ser Phe Ser Thr Ser Pro Thr Gly Gln Ser Pro Tyr Thr Tyr Gln
            20                  25                  30
Met His Gly Thr Thr Gly Phe Tyr Gln Gly Gly Asn Gly Leu Gly Asn
        35                  40                  45
Ala Ala Gly Phe Gly Ser Val His Gln Asp Tyr Pro Ser Tyr Pro Gly
    50                  55                  60
Phe Pro Gln Ser Gln Tyr Pro Gln Tyr Tyr Gly Ser Ser Tyr Asn Pro
65                  70                  75                  80
Pro Tyr Val Pro Ala Ser Ser Ile Cys Pro Ser Pro Leu Ser Thr Ser
                85                  90                  95
Thr Tyr Val Leu Gln Glu Ala Ser His Asn Val Pro Asn Gln Ser Ser
            100                 105                 110
Glu Ser Leu Ala Gly Glu Tyr Asn Thr His Asn Gly Pro Ser Thr Pro
        115                 120                 125
Ala Lys Glu Gly Asp Thr Asp Arg Pro His Arg Ala Ser Asp Gly Lys
    130                 135                 140
Leu Arg Gly Arg Ser Lys Arg Ser Ser Asp Pro Ser Pro Ala Gly Asp
145                 150                 155                 160
Asn Glu Ile Glu Arg Val Phe Val Trp Asp Leu Asp Glu Thr Ile Ile
                165                 170                 175
Ile Phe His Ser Leu Leu Thr Gly Thr Phe Ala Ser Arg Tyr Gly Lys
            180                 185                 190
Asp Thr Thr Thr Ser Val Arg Ile Gly Leu Met Met Glu Glu Met Ile
        195                 200                 205
Phe Asn Leu Ala Asp Thr His Leu Phe Phe Asn Asp Leu Glu Asp Cys
    210                 215                 220
Asp Gln Ile His Val Asp Asp Val Ser Ser Asp Asp Asn Gly Gln Asp
225                 230                 235                 240
Leu Ser Thr Tyr Asn Phe Ser Ala Asp Gly Phe His Ser Ser Ala Pro
                245                 250                 255
Gly Ala Asn Leu Cys Leu Gly Ser Gly Val His Gly Gly Val Asp Trp
            260                 265                 270
Met Arg Lys Leu Ala Phe Arg Tyr Arg Arg Val Lys Glu Met Tyr Asn
        275                 280                 285
Thr Tyr Lys Asn Asn Val Gly Gly Leu Ile Gly Thr Pro Lys Arg Glu
    290                 295                 300
Thr Trp Leu Gln Leu Arg Ala Glu Leu Glu Ala Leu Thr Asp Leu Trp
305                 310                 315                 320
Leu Thr His Ser Leu Lys Ala Leu Asn Leu Ile Asn Ser Arg Pro Asn
                325                 330                 335
Cys Val Asn Val Leu Val Thr Thr Thr Gln Leu Ile Pro Ala Leu Ala
            340                 345                 350
Lys Val Leu Leu Tyr Gly Leu Gly Ser Val Phe Pro Ile Glu Asn Ile
        355                 360                 365
Tyr Ser Ala Thr Lys Thr Gly Lys Glu Ser Cys Phe Glu Arg Ile Met
    370                 375                 380
Gln Arg Phe Gly Arg Lys Ala Val Tyr Val Val Ile Gly Asp Gly Val
385                 390                 395                 400
Glu Glu Glu Gln Gly Ala Lys Lys His Asn Met Pro Phe Trp Arg Ile
                405                 410                 415
Ser Cys His Ala Asp Leu Glu Ala Leu Arg His Ala Leu Glu Leu Glu
            420                 425                 430
Tyr Leu
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<210> 74
<211> 1907
<212> DNA
<213> Homo sapiens

<400> 74
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acatttttag caactacttc agtgcgatgt acagctcgga ggactccacc ctggcctctg 180
ttccccctgc tgccaccttt ggggccgatg acttggtact gaccctgagc aacccccaga 240
tgtcattgga gggtacagag aaggccagct ggttgggggga acagccccag ttctggtcga 300
agacgcaggt tctggactgg atcagctacc aagtggagaa gaacaagtac gacgcaagcg 360
ccattgactt ctcacgatgt gacatggatg gcgccaccct ctgcaattgt gcccttgagg 420
agctgcgtct ggtctttggg cctctggggg accaactcca tgcccagctg cgagacctca 480
cttccagctc ttctgatgag ctcagttgga tcattgagct gctggagaag gatggcatgg 540
ccttccagga ggccctagac ccagggccct ttgaccaggg cagccccttt gcccaggagc 600
tgctggacga cggtcagcaa gccagcccct accaccccgg cagctgtggc gcaggagccc 660
cctcccctgg cagctctgac gtctccaccg cagggactgg tgcttctcgg agctcccact 720
cctcagactc cggtggaagt gacgtggacc tggatcccac tgatggcaag ctcttcccca 780
gcgatggttt tcgtgactgc aagaaggggg atcccaagca cgggaagcgg aaacgaggcc 840
ggccccgaaa gctgagcaaa gagtactggg actgtctcga gggcaagaag agcaagcacg 900
cgcccagagg cacccacctg tgggagttca tccgggacat cctcatccac ccggagctca 960
acgagggcct catgaagtgg gagaatcggc atgaaggcgt cttcaagttc ctgcgctccg 1020
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tgagccgggc catgaggtac tactacaaac gggagatcct ggaacgggtg gatggccggc 1140
gactcgtcta caagtttggc aaaaactcaa gcggctggaa ggaggaagag gttctccaga 1200
gtcggaactg agggttggaa ctatacccgg gaccaaactc acggaccact cgaggcctgc 1260
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cttaaatgca gacaacacct tcttcctgca gacacttgga ctgagccaag gaggcttggg 1560
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tcccctcccc actcctctcc cacagagtgc tggactgttc caggccctcc agtgggctga 1800
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tccaataaag tgccttctgg gctttttcta aaaaaaaaaa aaaaaaa 1907

<210> 75
<211> 371
<212> PRT
<213> Homo sapiens

<400> 75
Met Ala Ala Thr Cys Glu Ile Ser Asn Ile Phe Ser Asn Tyr Phe Ser
1 5 10 15
Ala Met Tyr Ser Ser Glu Asp Ser Thr Leu Ala Ser Val Pro Pro Ala
20 25 30
Ala Thr Phe Gly Ala Asp Asp Leu Val Leu Thr Leu Ser Asn Pro Gln
35 40 45
Met Ser Leu Glu Gly Thr Glu Lys Ala Ser Trp Leu Gly Glu Gln Pro
50 55 60
Gln Phe Trp Ser Lys Thr Gln Val Leu Asp Trp Ile Ser Tyr Gln Val
65 70 75 80
Glu Lys Asn Lys Tyr Asp Ala Ser Ala Ile Asp Phe Ser Arg Cys Asp

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                85                  90                  95
Met Asp Gly Ala Thr Leu Cys Asn Cys Ala Leu Glu Glu Leu Arg Leu
            100                 105                 110
Val Phe Gly Pro Leu Gly Asp Gln Leu His Ala Gln Leu Arg Asp Leu
        115                 120                 125
Thr Ser Ser Ser Ser Asp Glu Leu Ser Trp Ile Ile Glu Leu Leu Glu
    130                 135                 140
Lys Asp Gly Met Ala Phe Gln Glu Ala Leu Asp Pro Gly Pro Phe Asp
145                 150                 155                 160
Gln Gly Ser Pro Phe Ala Gln Glu Leu Leu Asp Asp Gly Gln Gln Ala
                165                 170                 175
Ser Pro Tyr His Pro Gly Ser Cys Gly Ala Gly Ala Pro Ser Pro Gly
            180                 185                 190
Ser Ser Asp Val Ser Thr Ala Gly Thr Gly Ala Ser Arg Ser Ser His
        195                 200                 205
Ser Ser Asp Ser Gly Gly Ser Asp Val Asp Leu Asp Pro Thr Asp Gly
    210                 215                 220
Lys Leu Phe Pro Ser Asp Gly Phe Arg Asp Cys Lys Lys Gly Asp Pro
225                 230                 235                 240
Lys His Gly Lys Arg Lys Arg Gly Arg Pro Arg Lys Leu Ser Lys Glu
                245                 250                 255
Tyr Trp Asp Cys Leu Glu Gly Lys Lys Ser Lys His Ala Pro Arg Gly
            260                 265                 270
Thr His Leu Trp Glu Phe Ile Arg Asp Ile Leu Ile His Pro Glu Leu
        275                 280                 285
Asn Glu Gly Leu Met Lys Trp Glu Asn Arg His Glu Gly Val Phe Lys
    290                 295                 300
Phe Leu Arg Ser Glu Ala Val Ala Gln Leu Trp Gly Gln Lys Lys Lys
305                 310                 315                 320
Asn Ser Asn Met Thr Tyr Glu Lys Leu Ser Arg Ala Met Arg Tyr Tyr
                325                 330                 335
Tyr Lys Arg Glu Ile Leu Glu Arg Val Asp Gly Arg Arg Leu Val Tyr
            340                 345                 350
Lys Phe Gly Lys Asn Ser Ser Gly Trp Lys Glu Glu Glu Val Leu Gln
        355                 360                 365
Ser Arg Asn
    370


&lt;210&gt; 76
&lt;211&gt; 3951
&lt;212&gt; DNA
&lt;213&gt; Homo sapiens

&lt;220&gt;
&lt;221&gt; misc_feature
&lt;222&gt; (1)...(3951)
&lt;223&gt; n = A,T,C or G

&lt;400&gt; 76
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agctggctca agtacattag attcgctggc tgttatgatc agcacaacct tgttgcatgc 180
cagataaatg atcagatatt ctatagagta gttgcagaca ttgcgccggg agaggagctt 240
ctgctgttca tgaagagcga agactatccc catgaaacta tggcgccgga tatccacgaa 300
gaacggcaat atcgctgcga agactgtgac cagctctttg aatctaaggc tgaactagca 360
gatcaccaaa agtttccatg cagtactcct cactcagcat tttcaatggt tgaagaggac 420
tttcagcaaa aactcgaaag cgagaatgat ctccaagaga tacacacgat ccaggagtgt 480
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ttaattcgcc accagatgtc acatgacagt ggaaagcact atgaatgtga aaactgtgcc 660
aaggttttca cggaccctag caaccttcag cggcacattc gctctcagca tgtcggtgcc 720
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gatgagaagc ccttgactcc agtcccctcc aagcctccag tgacacctgc cacaagccaa 1020
gaccagcccc tggatctaag tatgggcagt aggagtagag ccagtgggac aaagctgact 1080
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aagcatgatt cttctgatta aaaactgtac tccatatttt atgctggttg tctgcaagct 3540
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ttaaaagaga gaangtaaat aacagactgt attcagttat tttgcccttt attgaggaac 3660
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ttacaacgtc gtgactggga aaaccctggg ttacccaact taatcgtctt n 3951

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<210> 77
<211> 718
<212> PRT
<213> Homo sapiens

<400> 77
Met Lys Ser Glu Asp Tyr Pro His Glu Thr Met Ala Pro Asp Ile His
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            20                  25                  30
Lys Ala Glu Leu Ala Asp His Gln Lys Phe Pro Cys Ser Thr Pro His
        35                  40                  45
Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser
    50                  55                  60
Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
65                  70                  75                  80
Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
                85                  90                  95
His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
            100                 105                 110
Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly
        115                 120                 125
Lys His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro Ser
    130                 135                 140
Asn Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala His
145                 150                 155                 160
Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys
                165                 170                 175
Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Ser Phe Ser
            180                 185                 190
Gln Ser Met Tyr Pro Phe Pro Asp Arg Asp Leu Arg Ser Leu Pro Leu
        195                 200                 205
Lys Met Glu Pro Gln Ser Pro Gly Glu Val Lys Lys Leu Gln Lys Gly
    210                 215                 220
Ser Ser Glu Ser Pro Phe Asp Leu Thr Thr Lys Arg Lys Asp Glu Lys
225                 230                 235                 240
Pro Leu Thr Pro Val Pro Ser Lys Pro Pro Val Thr Pro Ala Thr Ser
                245                 250                 255
Gln Asp Gln Pro Leu Asp Leu Ser Met Gly Ser Arg Ser Arg Ala Ser
            260                 265                 270
Gly Thr Lys Leu Thr Glu Pro Arg Lys Asn His Val Phe Gly Gly Lys
        275                 280                 285
Lys Gly Ser Asn Val Glu Ser Arg Pro Ala Ser Asp Gly Ser Leu Gln
    290                 295                 300
His Ala Arg Pro Thr Pro Phe Phe Met Asp Pro Ile Tyr Arg Val Glu
305                 310                 315                 320
Lys Arg Lys Leu Thr Asp Pro Leu Glu Ala Leu Lys Glu Lys Tyr Leu
                325                 330                 335
Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln Met Ser Ala Ile Glu
            340                 345                 350
Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala Leu Lys Pro Glu Ala
        355                 360                 365
Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe Asn Phe Arg Ala Pro
    370                 375                 380
Pro Asn Ala Leu Pro Glu Asn Leu Leu Arg Lys Gly Lys Glu Arg Tyr
385                 390                 395                 400
Thr Cys Arg Tyr Cys Gly Lys Ile Phe Pro Arg Ser Ala Asn Leu Thr
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405 410 415
Arg His Leu Arg Thr His Thr Gly Glu Gln Pro Tyr Arg Cys Lys Tyr
420 425 430
Cys Asp Arg Ser Phe Ser Ile Ser Ser Asn Leu Gln Arg His Val Arg
435 440 445
Asn Ile His Asn Lys Glu Lys Pro Phe Lys Cys His Leu Cys Asp Arg
450 455 460
Cys Phe Gly Gln Gln Thr Asn Leu Asp Arg His Leu Lys Lys His Glu
465 470 475 480
Asn Gly Asn Met Ser Gly Thr Ala Thr Ser Ser Pro His Ser Glu Leu
485 490 495
Glu Ser Thr Gly Ala Ile Leu Asp Asp Lys Glu Asp Ala Tyr Phe Thr
500 505 510
Glu Ile Arg Asn Phe Ile Gly Asn Ser Asn His Gly Ser Gln Ser Pro
515 520 525
Arg Asn Val Glu Glu Arg Met Asn Gly Ser His Phe Lys Asp Glu Lys
530 535 540
Ala Leu Val Thr Ser Gln Asn Ser Asp Leu Leu Asp Asp Glu Glu Val
545 550 555 560
Glu Asp Glu Val Leu Leu Asp Glu Glu Asp Glu Asp Asn Asp Ile Thr
565 570 575
Gly Lys Thr Gly Lys Glu Pro Val Thr Ser Asn Leu His Glu Gly Asn
580 585 590
Pro Glu Asp Asp Tyr Glu Glu Thr Ser Ala Leu Glu Met Ser Cys Lys
595 600 605
Thr Ser Pro Val Arg Tyr Lys Glu Glu Glu Tyr Lys Ser Gly Leu Ser
610 615 620
Ala Leu Asp His Ile Arg His Phe Thr Asp Ser Leu Lys Met Arg Lys
625 630 635 640
Met Glu Asp Asn Gln Tyr Ser Glu Ala Glu Leu Ser Ser Phe Ser Thr
645 650 655
Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu His Arg Lys Ser Lys
660 665 670
Ser Gln Ala Tyr Ala Met Met Leu Ser Leu Ser Asp Lys Glu Ser Leu
675 680 685
His Ser Thr Ser His Ser Ser Ser Asn Val Trp His Ser Met Ala Arg
690 695 700
Ala Ala Ala Glu Ser Ser Ala Ile Gln Ser Ile Ser His Val
705 710 715

<210> 78
<211> 4950
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(4950)
<223> n = A,T,C or G

<400> 78
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atcttagacg aattttacaa tgtgaagttc tgcatagatg ccagtcaacc agatgttgga 120
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Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser
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Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
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Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
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His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
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Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
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Cys His Lys Ser Tyr Thr Gln Phe Ser Asn Leu Cys Arg His Lys Arg
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Met His Ala Asp Cys Arg Thr Gln Ile Lys Cys Lys Asp Cys Gly Gln
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Gly Lys Asn His Phe Ala Ala Gly Gly Phe Phe Gly Gln Gly Ile Ser
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Ser Ser Pro Val Lys Gly Leu Ser Ser Thr Glu Gln Thr Asn Lys Ser
325 330 335
Gln Ser Pro Leu Met Thr His Pro Gln Ile Leu Pro Ala Thr Gln Asp
340 345 350
Ile Leu Lys Ala Leu Ser Lys His Pro Ser Val Gly Asp Asn Lys Pro
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370 375 380
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Arg Thr His Thr Gly Glu Gln Pro Tyr Arg Cys Lys Tyr Cys Asp Arg
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785 790 795 800
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Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu Ser
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Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu Cys
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Asp Gln Val Phe Leu Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
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His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala Phe
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Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Ser Phe Ser
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Ile Phe Pro Arg Ser Ala Asn Leu Thr Arg His Leu Arg Thr His Thr
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65 70 75 80
Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu Ser
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Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser Gly
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Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu Lys
165 170 175
Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu Val
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Cys His Lys Ser Tyr Thr Gln Phe Ser Asn Leu Cys Arg His Lys Arg
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Ile Asn Ile Pro Ser Pro Glu His Ser Asn Thr Ile Asp Val Cys Asn
225                 230                 235                 240
Thr Val Asp Ile Lys Thr Glu Asp Leu Ser Asp Ser Leu Pro Pro Val
                245                 250                 255
Cys Asp Thr Val Ala Thr Asp Leu Cys Ser Thr Gly Ile Asp Ile Cys
            260                 265                 270
Ser Phe Ser Glu Asp Ile Lys Pro Gly Asp Ser Leu Leu Leu Ser Val
        275                 280                 285
Glu Glu Val Leu Arg Ser Leu Glu Thr Val Ser Asn Thr Glu Val Cys
    290                 295                 300
Cys Pro Asn Leu Gln Pro Asn Leu Glu Ala Thr Val Ser Asn Gly Pro
305                 310                 315                 320
Phe Leu Gln Leu Ser Ser Gln Ser Leu Ser His Asn Val Phe Met Ser
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325 330 335
Thr Ser Pro Ala Leu His Gly Leu Ser Cys Thr Ala Ala Thr Pro Lys
340 345 350
Ile Ala Lys Leu Asn Arg Lys Arg Ser Arg Ser Glu Ser Asp Ser Glu
355 360 365
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Gly Ala Ser Ala Pro Val Thr Val Lys Arg Glu Ser Lys Ile Ser Leu
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Gln Pro Ile Ala Thr Val Pro Asn Gly Gly Thr Thr Pro Lys Ile Ser
405 410 415
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420 425 430
Gly Ser Lys Lys Ser His Ser Lys Thr Lys Pro Gly Ile Leu Lys Lys
435 440 445
Asp Lys Ala Val Lys Glu Lys Ile Pro Ser His His Phe Met Pro Gly
450 455 460
Ser Pro Thr Lys Thr Val Tyr Lys Lys Pro Gln Glu Lys Lys Gly Cys
465 470 475 480
Lys Cys Gly Arg Ala Thr Gln Asn Pro Ser Val Leu Thr Cys Arg Gly
485 490 495
Gln Arg Cys Pro Cys Tyr Ser Asn Arg Lys Ala Cys Leu Asp Cys Ile
500 505 510
Cys Arg Gly Cys Gln Asn Ser Tyr Met Ala Asn Gly Glu Lys Lys Leu
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Glu Ala Phe Ala Val Pro Glu Lys Ala Leu Glu Gln Thr Arg Leu Thr
530 535 540
Leu Gly Ile Asn Val Thr Ser Ile Ala Val Arg Asn Ala Ser Thr Ser
545 550 555 560
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Ala Ser Thr His Asp Asp Lys Ser Leu Asp Glu Ala Ile Asp Met Arg
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Phe Asp Cys
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<210> 86
<211> 1385
<212> DNA
<213> Homo sapiens

<400> 86
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<211> 252
<212> PRT
<213> Homo sapiens

<400> 87
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35 40 45
Asp Phe Tyr Val His Thr Val Met Thr Cys Tyr Phe Ser Leu Phe Gly
50 55 60
Ile Asp Asn Met Ala Pro Ser Pro Gly His Ile Leu Arg Val Tyr Gly
65 70 75 80
Gly Val Leu Pro Trp Ser Val Ala Leu Asp Trp Leu Thr Glu Lys Pro
85 90 95
Glu Leu Phe Gln Leu Ala Leu Lys Ala Phe Arg Tyr Thr Leu Lys Leu
100 105 110
Met Ile Asp Lys Ala Ser Leu Gly Pro Ile Glu Asp Phe Arg Glu Leu
115 120 125
Ile Lys Tyr Leu Glu Glu Tyr Glu Arg Asp Trp Tyr Ile Gly Leu Val
130 135 140
Ser Asp Glu Lys Trp Lys Glu Ala Ile Leu Gln Glu Lys Pro Tyr Leu
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Phe Ser Leu Gly Tyr Asp Ser Asn Met Gly Ile Tyr Thr Gly Arg Val
165 170 175
Leu Ser Leu Gln Glu Leu Leu Ile Gln Val Gly Lys Leu Asn Pro Glu
180 185 190
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195 200 205
Thr Asn Asp Asp Glu Glu Arg Tyr Ser Ile Gln Ala His Pro Leu Leu
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<211> 4660
<212> DNA
<213> Homo sapiens

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<210> 89
<211> 538
<212> PRT
<213> Homo sapiens

<400> 89

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Ile His Gln Gln Pro Asn Pro Gly Val His Tyr Glu Tyr Val Ile Met
        35                  40                  45
Gly Thr Asn Ala Ile Ser Pro Gln Val Pro Pro His Arg Arg Pro Gly
    50                  55                  60
Glu Pro Phe Asn Gly Gln Met Val Thr Glu Gly Arg Ser Gln Glu Glu
65                  70                  75                  80
Gly Glu Gln Lys Gly Arg Asn Glu Glu Lys Glu Asp Leu Arg Gly Glu
                85                  90                  95
Ala Pro Glu Met Phe Thr Ser Glu Ser Ala Gln Thr Phe Pro Val Arg
            100                 105                 110
His Pro Asp Arg Phe Ser Pro His Arg Pro Asp Asn Leu Val Pro Pro
        115                 120                 125
Ala Pro Gln Pro Pro Arg Arg Ser Arg Asp His Asn Trp Lys Gln Leu
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Gly Thr Thr Glu Cys Ser Thr Thr Cys Gly Lys Gly Ser Gln Tyr Pro
145                 150                 155                 160
Ile Phe Arg Cys Val His Arg Ser Thr His Glu Glu Ala Pro Glu Ser
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Tyr Cys Asp Ser Ser Met Lys Pro Thr Pro Glu Glu Glu Pro Cys Asn
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Ile Phe Pro Cys Pro Ala Phe Trp Asp Ile Gly Glu Trp Ser Glu Cys
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Ser Lys Thr Cys Gly Leu Gly Met Gln His Arg Gln Val Leu Cys Arg
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Gln Val Tyr Ala Asn Arg Ser Leu Thr Val Gln Pro Tyr Arg Cys Gln
225                 230                 235                 240
His Leu Glu Lys Pro Glu Thr Thr Ser Thr Cys Gln Leu Lys Ile Cys
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Ser Glu Trp Gln Ile Arg Thr Asp Trp Thr Ser Cys Ser Val Pro Cys
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Glu Trp Ser Glu Arg Ser Ser Ala Glu Cys Gly Ala Gly Val Arg Thr
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Arg Ser Val Val Cys Met Thr Asn His Val Ser Ser Leu Pro Leu Glu
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Gly Cys Gly Asn Asn Arg Pro Ala Glu Ala Thr Pro Cys Asp Asn Gly
        355                 360                 365
Pro Cys Thr Gly Lys Val Glu Trp Phe Ala Gly Ser Trp Ser Gln Cys
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385                 390                 395                 400
Arg Lys Asn Ala Asp Thr Phe Glu Val Leu Asp Pro Ser Glu Cys Ser
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Phe Leu Glu Lys Pro Pro Ser Gln Gln Ser Cys His Leu Lys Pro Cys
            420                 425                 430
Gly Ala Lys Trp Phe Ser Thr Glu Trp Ser Met Cys Ser Lys Ser Cys
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Gln Gly Gly Phe Arg Val Arg Glu Val Arg Cys Leu Ser Asp Asp Met
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Thr Leu Ser Asn Leu Cys Asp Pro Gln Leu Lys Pro Glu Glu Arg Glu
465                 470                 475                 480
Ser Cys Asn Pro Gln Asp Cys Val Pro Glu Val Asp Glu Asn Cys Lys
                485                 490                 495
Asp Lys Tyr Tyr Asn Cys Asn Val Val Val Gln Ala Arg Leu Cys Val
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<210> 90
<211> 4793
<212> DNA
<213> Homo sapiens

<400> 90

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<210> 91
<211> 625
<212> PRT
<213> Homo sapiens

<400> 91
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            20                  25                  30
Asp Glu Ala Trp Lys Ser Tyr Leu Glu Asn Pro Leu Thr Ala Ala Thr
        35                  40                  45
Lys Ala Met Met Ile Ile Asn Gly Asp Glu Asp Ser Ala Ala Ala Leu
    50                  55                  60
Gly Leu Leu Tyr Asp Tyr Tyr Lys Val Pro Arg Asp Lys Arg Leu Leu
65                  70                  75                  80
Ser Val Ser Lys Ala Ser Asp Ser Gln Glu Asp Gln Glu Lys Arg Asn
                85                  90                  95
Cys Leu Gly Thr Ser Glu Ala Gln Ser Asn Leu Ser Gly Gly Glu Asn
            100                 105                 110
Arg Val Gln Val Leu Lys Thr Val Pro Val Asn Leu Ser Leu Asn Gln
        115                 120                 125
Asp His Leu Glu Asn Ser Lys Arg Glu Gln Tyr Ser Ile Ser Phe Pro
    130                 135                 140
Glu Ser Ser Ala Ile Ile Pro Val Ser Gly Ile Thr Val Val Lys Ala
145                 150                 155                 160
Glu Asp Phe Thr Pro Val Phe Met Ala Pro Pro Val His Tyr Pro Arg
                165                 170                 175
Gly Asp Gly Glu Glu Gln Arg Val Val Ile Phe Glu Gln Thr Gln Tyr
            180                 185                 190
Asp Val Pro Ser Leu Ala Thr His Ser Ala Tyr Leu Lys Asp Asp Gln
        195                 200                 205
Arg Ser Thr Pro Asp Ser Thr Tyr Ser Glu Ser Phe Lys Asp Ala Ala
    210                 215                 220
Thr Glu Lys Phe Arg Ser Ala Ser Val Gly Ala Glu Glu Tyr Met Tyr
225                 230                 235                 240
Asp Gln Thr Ser Ser Gly Thr Phe Gln Tyr Thr Leu Glu Ala Thr Lys
                245                 250                 255
Ser Leu Arg Gln Lys Gln Gly Glu Gly Pro Met Thr Tyr Leu Asn Lys
            260                 265                 270
Gly Gln Phe Tyr Ala Ile Thr Leu Ser Glu Thr Gly Asp Asn Lys Cys
        275                 280                 285
Phe Arg His Pro Ile Ser Lys Val Arg Ser Val Val Met Val Val Phe
    290                 295                 300
Ser Glu Asp Lys Asn Arg Asp Glu Gln Leu Lys Tyr Trp Lys Tyr Trp
305                 310                 315                 320
His Ser Arg Gln His Thr Ala Lys Gln Arg Val Leu Asp Ile Ala Asp
                325                 330                 335
Tyr Lys Glu Ser Phe Asn Thr Ile Gly Asn Ile Glu Glu Ile Ala Tyr
            340                 345                 350
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Asn Ala Val Ser Phe Thr Trp Asp Val Asn Glu Glu Ala Lys Ile Phe
        355                 360                 365
Ile Thr Val Asn Cys Leu Ser Thr Asp Phe Ser Ser Gln Lys Gly Val
    370                 375                 380
Lys Gly Leu Pro Leu Met Ile Gln Ile Asp Thr Tyr Ser Tyr Asn Asn
385                 390                 395                 400
Arg Ser Asn Lys Pro Ile His Arg Ala Tyr Cys Gln Ile Lys Val Phe
                405                 410                 415
Cys Asp Lys Gly Ala Glu Arg Lys Ile Arg Asp Glu Glu Gln Lys Gln
            420                 425                 430
Asn Arg Lys Asn Gly Lys Gly Gln Ala Ser Gln Thr Gln Cys Asn Ser
        435                 440                 445
Ser Ser Asp Gly Lys Leu Ala Ala Ile Pro Leu Gln Lys Lys Ser Asp
    450                 455                 460
Ile Thr Tyr Phe Lys Thr Met Pro Asp Leu His Ser Gln Pro Val Leu
465                 470                 475                 480
Phe Ile Pro Asp Val His Phe Ala Asn Leu Gln Arg Thr Gly Gln Val
                485                 490                 495
Tyr Tyr Asn Thr Asp Asp Glu Arg Glu Gly Gly Ser Val Leu Val Lys
            500                 505                 510
Arg Met Phe Arg Pro Met Glu Glu Glu Phe Gly Pro Val Pro Ser Lys
        515                 520                 525
Gln Met Lys Glu Glu Gly Thr Lys Arg Val Leu Leu Tyr Val Arg Lys
    530                 535                 540
Glu Thr Asp Asp Val Phe Asp Ala Leu Met Leu Lys Ser Pro Thr Val
545                 550                 555                 560
Met Gly Leu Met Glu Ala Ile Ser Glu Lys Tyr Gly Leu Pro Val Glu
                565                 570                 575
Lys Ile Ala Lys Leu Tyr Lys Lys Ser Lys Lys Gly Ile Leu Val Asn
            580                 585                 590
Met Asp Asp Asn Ile Ile Glu His Tyr Ser Asn Glu Asp Thr Phe Ile
        595                 600                 605
Leu Asn Met Glu Ser Met Val Glu Gly Phe Lys Val Thr Leu Met Glu
    610                 615                 620
Ile
625
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<210> 92
<211> 2085
<212> DNA
<213> Homo sapiens

<400> 92

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tgattcagaa ggagcaagag attttcgaga ggaccgaaga agcagagggc attttggatc 360
cccaggagtc ggaaatgtta aactttaatg agaagtgcac tcggagccca ctactgaccc 420
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gtgcctataa ggtgggcgtg gcttcaggcc acctgccccg caagggttct ggcagtgact 720
gccgtctggg ccacaatgcc ttctcctggg tcttctctcg ctatgatcag gagtttcgtt 780
tctcacacaa tgggcagcac gagcccctgg ggctgctgcg gggcccagcc cagctgggtg 840
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<210> 93
<211> 301
<212> PRT
<213> Homo sapiens

<400> 93

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            20                  25                  30
Gly Glu Glu Glu Arg Ala His Gln Ser Ile Leu Thr Gln Arg Val His
        35                  40                  45
Trp Ala Glu Ala Leu Gln Lys Leu Asp Thr Ile Arg Thr Gly Leu Val
    50                  55                  60
Gly Met Leu Thr His Leu Asp Asp Leu Gln Leu Ile Gln Lys Glu Gln
65                  70                  75                  80
Glu Ile Phe Glu Arg Thr Glu Glu Ala Glu Gly Ile Leu Asp Pro Gln
                85                  90                  95
Glu Ser Glu Met Leu Asn Phe Asn Glu Lys Cys Thr Arg Ser Pro Leu
            100                 105                 110
Leu Thr Gln Leu Trp Ala Thr Ala Val Leu Gly Ser Leu Ser Gly Thr
        115                 120                 125
Glu Asp Ile Arg Ile Asp Glu Arg Thr Val Ser Pro Phe Leu Gln Leu
    130                 135                 140
Ser Asp Asp Arg Lys Thr Leu Thr Phe Ser Thr Lys Lys Ser Lys Ala
145                 150                 155                 160
Cys Ala Asp Gly Pro Glu Arg Phe Asp His Trp Pro Asn Ala Leu Ala
                165                 170                 175
Ala Thr Ser Phe Gln Asn Gly Leu His Ala Trp Met Val Asn Val Gln
            180                 185                 190
Asn Ser Cys Ala Tyr Lys Val Gly Val Ala Ser Gly His Leu Pro Arg
        195                 200                 205
Lys Gly Ser Gly Ser Asp Cys Arg Leu Gly His Asn Ala Phe Ser Trp
    210                 215                 220
Val Phe Ser Arg Tyr Asp Gln Glu Phe Arg Phe Ser His Asn Gly Gln
225                 230                 235                 240
```

His Glu Pro Leu Gly Leu Leu Arg Gly Pro Ala Gln Leu Gly Val Val
245 250 255
Leu Asp Leu Gln Val Gln Glu Leu Leu Phe Tyr Glu Pro Ala Ser Gly
260 265 270
Ile Val Leu Cys Ala His His Val Ser Phe Pro Gly Pro Leu Phe Pro
275 280 285
Val Phe Ala Val Ala Asp Gln Thr Ile Ser Ile Val Arg
290 295 300

<210> 94
<211> 2317
<212> DNA
<213> Homo sapiens

<400> 94
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<210> 95
<211> 626

<212> PRT
<213> Homo sapiens

<400> 95
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Leu Thr Cys Leu Cys Pro Gln Cys Leu Ser Val Glu Asp Ala Leu Gly
35 40 45
Leu Gly Glu Pro Glu Gly Ser Gly Leu Pro Pro Gly Pro Val Leu Glu
50 55 60
Ala Arg Tyr Val Ala Arg Leu Ser Ala Ala Ala Val Leu Tyr Leu Ser
65 70 75 80
Asn Pro Glu Gly Thr Cys Glu Asp Ala Arg Ala Gly Leu Trp Ala Ser
85 90 95
His Ala Asp His Leu Leu Ala Leu Leu Glu Ser Pro Lys Ala Leu Thr
100 105 110
Pro Gly Leu Ser Trp Leu Leu Gln Arg Met Gln Ala Arg Ala Ala Gly
115 120 125
Gln Thr Pro Lys Thr Ala Cys Val Asp Ile Pro Gln Leu Leu Glu Glu
130 135 140
Ala Val Gly Ala Gly Ala Pro Gly Ser Ala Gly Gly Val Leu Ala Ala
145 150 155 160
Leu Leu Asp His Val Arg Ser Gly Ser Cys Phe His Ala Leu Pro Ser
165 170 175
Pro Gln Tyr Phe Val Asp Phe Val Phe Gln Gln His Ser Ser Glu Val
180 185 190
Pro Met Thr Leu Ala Glu Leu Ser Ala Leu Met Gln Arg Leu Gly Val
195 200 205
Gly Arg Glu Ala His Ser Asp His Ser His Arg His Arg Gly Ala Ser
210 215 220
Ser Arg Asp Pro Val Pro Leu Ile Ser Ser Ser Asn Ser Ser Ser Val
225 230 235 240
Trp Asp Thr Val Cys Leu Ser Ala Arg Asp Val Met Ala Ala Tyr Gly
245 250 255
Leu Ser Glu Gln Ala Gly Val Thr Pro Glu Ala Trp Ala Gln Leu Ser
260 265 270
Pro Ala Leu Leu Gln Gln Gln Leu Ser Gly Ala Tyr Thr Ser Gln Ser
275 280 285
Arg Pro Pro Val Gln Asp Gln Leu Ser Gln Ser Glu Arg Tyr Leu Tyr
290 295 300
Gly Ser Leu Ala Thr Leu Leu Ile Cys Leu Cys Ala Val Phe Gly Leu
305 310 315 320
Leu Leu Leu Thr Cys Thr Gly Cys Arg Gly Val Ala His Tyr Ile Leu
325 330 335
Gln Thr Phe Leu Ser Leu Ala Val Gly Ala Leu Thr Gly Asp Ala Val
340 345 350
Leu His Leu Thr Pro Lys Val Leu Gly Leu His Thr His Ser Glu Glu
355 360 365
Gly Leu Ser Pro Gln Pro Thr Trp Arg Leu Leu Ala Met Leu Ala Gly
370 375 380
Leu Tyr Ala Phe Phe Leu Phe Glu Asn Leu Phe Asn Leu Leu Leu Pro
385 390 395 400
Arg Asp Pro Glu Asp Leu Glu Asp Gly Pro Cys Gly His Ser Ser His
405 410 415
Ser His Gly Gly His Ser His Gly Val Ser Leu Gln Leu Ala Pro Ser
420 425 430

```
Glu Leu Arg Gln Pro Lys Pro Pro His Glu Gly Ser Arg Ala Asp Leu
        435                 440                 445
Val Ala Glu Glu Ser Pro Glu Leu Leu Asn Pro Glu Pro Arg Arg Leu
    450                 455                 460
Ser Pro Glu Leu Arg Leu Leu Pro Tyr Met Ile Thr Leu Gly Asp Ala
465                 470                 475                 480
Val His Asn Phe Ala Asp Gly Leu Ala Val Gly Ala Ala Phe Ala Ser
                485                 490                 495
Ser Trp Lys Thr Gly Leu Ala Thr Ser Leu Ala Val Phe Cys His Glu
            500                 505                 510
Leu Pro His Glu Leu Gly Asp Phe Ala Ala Leu Leu His Ala Gly Leu
        515                 520                 525
Ser Val Arg Gln Ala Leu Leu Leu Asn Leu Ala Ser Ala Leu Thr Ala
    530                 535                 540
Phe Ala Gly Leu Thr Trp His Ser Arg Leu Glu Ser Ala Arg Arg Ala
545                 550                 555                 560
Arg Pro Gly Ser Trp Gln Trp Pro Pro Ala Cys Ser Leu Arg Ser Thr
                565                 570                 575
Leu Arg His Ala Pro Gly Asp Val Glu Ser Thr Gly Pro Ala Ala Pro
            580                 585                 590
Gly Ser Ser Ser Cys Cys Thr Thr Trp Ala Cys Trp Ala Ala Gly Pro
        595                 600                 605
Ser Cys Cys Cys Cys Pro Cys Thr Arg Met Thr Ser Pro Ser Asp Thr
    610                 615                 620
Leu Pro
625
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<210> 96
<211> 2761
<212> DNA
<213> Homo sapiens

<400> 96

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cggggagaat gtggccaagt ttattattaa ttcatacccc aaatattttc agaaggacat 420
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<210> 97
<211> 422
<212> PRT
<213> Homo sapiens

<400> 97
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 1               5                  10                  15
Trp Leu Gly Leu Arg Ser Arg Leu Gly Gln Pro Leu Thr Gly Arg Arg
            20                  25                  30
Ala Gly Leu Cys Glu Gln Ala Arg Ser Cys Arg Phe Tyr Ser Gly Ser
        35                  40                  45
Ala Thr Leu Ser Lys Val Glu Gly Thr Asp Val Thr Gly Ile Glu Glu
    50                  55                  60
Val Val Ile Pro Lys Lys Lys Thr Trp Asp Lys Val Ala Val Leu Gln
65                  70                  75                  80
Ala Leu Ala Ser Thr Val Asn Arg Asp Thr Thr Ala Val Pro Tyr Val
                85                  90                  95
Phe Gln Asp Asp Pro Tyr Leu Met Pro Ala Ser Ser Leu Glu Ser Arg
            100                 105                 110
Ser Phe Leu Leu Ala Lys Lys Ser Gly Glu Asn Val Ala Lys Phe Ile
        115                 120                 125
Ile Asn Ser Tyr Pro Lys Tyr Phe Gln Lys Asp Ile Ala Glu Pro His
    130                 135                 140
Ile Pro Cys Leu Met Pro Glu Tyr Phe Glu Pro Gln Ile Lys Asp Ile
145                 150                 155                 160
Ser Glu Ala Ala Leu Lys Glu Arg Ile Glu Leu Arg Lys Val Lys Ala
                165                 170                 175
Ser Val Asp Met Phe Asp Gln Leu Leu Gln Ala Gly Thr Thr Val Ser
            180                 185                 190
Leu Glu Thr Thr Asn Ser Leu Leu Asp Leu Leu Cys Tyr Tyr Gly Asp
        195                 200                 205
Gln Glu Pro Ser Thr Asp Tyr His Phe Gln Gln Thr Gly Gln Ser Glu
    210                 215                 220
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Ala Leu Glu Glu Glu Asn Asp Glu Thr Ser Arg Arg Lys Ala Gly His
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Gln Phe Gly Val Thr Trp Arg Ala Lys Asn Asn Ala Glu Arg Ile Phe
245 250 255
Ser Leu Met Pro Glu Lys Asn Glu His Ser Tyr Cys Thr Met Ile Arg
260 265 270
Gly Met Val Lys His Arg Ala Tyr Glu Gln Ala Leu Asn Leu Tyr Thr
275 280 285
Glu Leu Leu Asn Asn Arg Leu His Ala Asp Val Tyr Thr Phe Asn Ala
290 295 300
Leu Ile Glu Ala Thr Val Cys Ala Ile Asn Glu Lys Phe Glu Glu Lys
305 310 315 320
Trp Ser Lys Ile Leu Glu Leu Leu Arg His Met Val Ala Gln Lys Val
325 330 335
Lys Pro Asn Leu Gln Thr Phe Asn Thr Ile Leu Lys Cys Leu Arg Arg
340 345 350
Phe His Val Phe Ala Arg Ser Pro Ala Leu Gln Val Leu Arg Glu Met
355 360 365
Lys Ala Ile Gly Ile Glu Pro Ser Leu Ala Thr Tyr His His Ile Ile
370 375 380
Arg Leu Phe Asp Gln Pro Gly Asp Pro Leu Lys Arg Ser Ser Phe Ile
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Ile Tyr Asp Ile Met Asn Glu Leu Met Gly Lys Arg Phe Ser Pro Lys
405 410 415
Asp Pro Asp Asp Gly Ile
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<210> 98
<211> 2757
<212> DNA
<213> Homo sapiens

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cggggagaat gtggccaagt ttattattaa ttcatacccc aaatattttc agaaggacat 420
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aagtgaagcc gccctgaagg aacgaattga gctcagaaaa gtcaaagcct ctgtggacat 540
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<210> 99
<211> 697
<212> PRT
<213> Homo sapiens

<400> 99

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            20                  25                  30
Ala Gly Leu Cys Glu Gln Ala Arg Ser Cys Arg Phe Tyr Ser Gly Ser
        35                  40                  45
Ala Thr Leu Ser Lys Val Glu Gly Thr Asp Val Thr Gly Ile Glu Glu
    50                  55                  60
Val Val Ile Pro Lys Lys Lys Thr Trp Asp Lys Val Ala Val Leu Gln
65                  70                  75                  80
Ala Leu Ala Ser Thr Val Asn Arg Asp Thr Thr Ala Val Pro Tyr Val
                85                  90                  95
Phe Gln Asp Asp Pro Tyr Leu Met Pro Ala Ser Ser Leu Glu Ser Arg
            100                 105                 110
Ser Phe Leu Leu Ala Lys Lys Ser Gly Glu Asn Val Ala Lys Phe Ile
        115                 120                 125
Ile Asn Ser Tyr Pro Lys Tyr Phe Gln Lys Asp Ile Ala Glu Pro His
    130                 135                 140
Ile Pro Cys Leu Met Pro Glu Tyr Phe Glu Pro Gln Ile Lys Asp Ile
145                 150                 155                 160
Ser Glu Ala Ala Leu Lys Glu Arg Ile Glu Leu Arg Lys Val Lys Ala
                165                 170                 175
Ser Val Asp Met Phe Asp Gln Leu Leu Gln Ala Gly Thr Thr Val Ser
            180                 185                 190
Leu Glu Thr Thr Asn Ser Leu Leu Asp Leu Leu Cys Tyr Tyr Gly Asp
        195                 200                 205
Gln Glu Pro Ser Thr Asp Tyr His Phe Gln Gln Thr Gly Gln Ser Glu
    210                 215                 220
Ala Leu Glu Glu Glu Asn Asp Glu Thr Ser Arg Arg Lys Ala Gly His
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225                 230                 235                 240
Gln Phe Gly Val Thr Trp Arg Ala Lys Asn Asn Ala Glu Arg Ile Phe
                245                 250                 255
Ser Leu Met Pro Glu Lys Asn Glu His Ser Tyr Cys Thr Met Ile Arg
            260                 265                 270
Gly Met Val Lys His Arg Ala Tyr Glu Gln Ala Leu Asn Leu Tyr Thr
        275                 280                 285
Glu Leu Leu Asn Asn Arg Leu His Ala Asp Val Tyr Thr Phe Asn Ala
    290                 295                 300
Leu Ile Glu Ala Thr Val Cys Ala Ile Asn Glu Lys Phe Glu Glu Lys
305                 310                 315                 320
Trp Ser Lys Ile Leu Glu Leu Leu Arg His Met Val Ala Gln Lys Val
                325                 330                 335
Lys Pro Asn Leu Gln Thr Phe Asn Thr Ile Leu Lys Cys Leu Arg Arg
            340                 345                 350
Phe His Val Phe Ala Arg Ser Pro Ala Leu Gln Val Leu Arg Glu Met
        355                 360                 365
Lys Ala Ile Gly Ile Glu Pro Ser Leu Ala Thr Tyr His His Ile Ile
    370                 375                 380
Arg Leu Phe Asp Gln Pro Gly Asp Pro Leu Lys Arg Ser Ser Phe Ile
385                 390                 395                 400
Ile Tyr Asp Ile Met Asn Glu Leu Met Gly Lys Arg Phe Ser Pro Lys
                405                 410                 415
Asp Pro Asp Asp Asp Lys Phe Phe Gln Ser Ala Met Ser Ile Cys Ser
            420                 425                 430
Ser Leu Arg Asp Leu Glu Leu Ala Tyr Gln Val His Gly Leu Leu Lys
        435                 440                 445
Thr Gly Asp Asn Trp Lys Phe Ile Gly Pro Asp Gln His Arg Asn Phe
    450                 455                 460
Tyr Tyr Ser Lys Phe Phe Asp Leu Ile Cys Leu Met Glu Gln Ile Asp
465                 470                 475                 480
Val Thr Leu Lys Trp Tyr Glu Asp Leu Ile Pro Ser Ala Tyr Phe Pro
                485                 490                 495
His Ser Gln Thr Met Ile His Leu Leu Gln Ala Leu Asp Val Ala Asn
            500                 505                 510
Arg Leu Glu Val Ile Pro Lys Ile Trp Lys Asp Ser Lys Glu Tyr Gly
        515                 520                 525
His Thr Phe Arg Ser Asp Leu Arg Glu Glu Ile Leu Met Leu Met Ala
    530                 535                 540
Arg Asp Lys His Pro Pro Glu Leu Gln Val Ala Phe Ala Asp Cys Ala
545                 550                 555                 560
Ala Asp Ile Lys Ser Ala Tyr Glu Ser Gln Pro Ile Arg Gln Thr Ala
                565                 570                 575
Gln Asp Trp Pro Ala Thr Ser Leu Asn Cys Ile Ala Ile Leu Phe Leu
            580                 585                 590
Arg Ala Gly Arg Thr Gln Glu Ala Trp Lys Met Leu Gly Leu Phe Arg
        595                 600                 605
Lys His Asn Lys Ile Pro Arg Ser Glu Leu Leu Asn Glu Leu Met Asp
    610                 615                 620
Ser Ala Lys Val Ser Asn Ser Pro Ser Gln Ala Ile Glu Val Val Glu
625                 630                 635                 640
Leu Ala Ser Ala Phe Ser Leu Pro Ile Cys Glu Gly Leu Thr Gln Arg
                645                 650                 655
Val Met Ser Asp Phe Ala Ile Asn Gln Glu Gln Lys Glu Ala Leu Ser
            660                 665                 670
Asn Leu Thr Ala Leu Thr Ser Asp Ser Asp Thr Asp Ser Ser Ser Asp
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Ser Asp Ser Asp Thr Ser Glu Gly Lys
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690 695

<210> 100
<211> 1940
<212> DNA
<213> Homo sapiens

<400> 100
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attgattgaa gcaacagtat gtgcgataaa tgagaaattt gaggaaaaat ggagtaaaat 180
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aatgaatgaa ttaatgggaa agagattttc tccaaaggac ccggatgatg gcatataagt 480
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<210> 101
<211> 280
<212> PRT
<213> Homo sapiens

<400> 101
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Leu Arg Asp Leu Glu Leu Ala Tyr Gln Val His Gly Leu Leu Lys Thr
20 25 30
Gly Asp Asn Trp Lys Phe Ile Gly Pro Asp Gln His Arg Asn Phe Tyr
35 40 45
Tyr Ser Lys Phe Phe Asp Leu Ile Cys Leu Met Glu Gln Ile Asp Val
50 55 60
Thr Leu Lys Trp Tyr Glu Asp Leu Ile Pro Ser Ala Tyr Phe Pro His

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65                  70                  75                  80
Ser Gln Thr Met Ile His Leu Leu Gln Ala Leu Asp Val Ala Asn Arg
                85                  90                  95
Leu Glu Val Ile Pro Lys Ile Trp Lys Asp Ser Lys Glu Tyr Gly His
            100                 105                 110
Thr Phe Arg Ser Asp Leu Arg Glu Glu Ile Leu Met Leu Met Ala Arg
        115                 120                 125
Asp Lys His Pro Pro Glu Leu Gln Val Ala Phe Ala Asp Cys Ala Ala
    130                 135                 140
Asp Ile Lys Ser Ala Tyr Glu Ser Gln Pro Ile Arg Gln Thr Ala Gln
145                 150                 155                 160
Asp Trp Pro Ala Thr Ser Leu Asn Cys Ile Ala Ile Leu Phe Leu Arg
                165                 170                 175
Ala Gly Arg Thr Gln Glu Ala Trp Lys Met Leu Gly Leu Phe Arg Lys
            180                 185                 190
His Asn Lys Ile Pro Arg Ser Glu Leu Leu Asn Glu Leu Met Asp Ser
        195                 200                 205
Ala Lys Val Ser Asn Ser Pro Ser Gln Ala Ile Glu Val Val Glu Leu
    210                 215                 220
Ala Ser Ala Phe Ser Leu Pro Ile Cys Glu Gly Leu Thr Gln Arg Val
225                 230                 235                 240
Met Ser Asp Phe Ala Ile Asn Gln Glu Gln Lys Glu Ala Leu Ser Asn
                245                 250                 255
Leu Thr Ala Leu Thr Ser Asp Ser Asp Thr Asp Ser Ser Ser Asp Ser
            260                 265                 270
Asp Ser Asp Thr Ser Glu Gly Lys
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<210> 102
<211> 1853
<212> DNA
<213> Homo sapiens

<400> 102

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<210> 103
<211> 414
<212> PRT
<213> Homo sapiens

<400> 103
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            20                  25                  30
Ala Glu Ser Leu Ser Pro Ile Gly Asp Met Lys Val Lys Gly Glu Ala
        35                  40                  45
Pro Ala Asn Ser Gly Ala Pro Ala Gly Ala Ala Gly Arg Ala Lys Gly
    50                  55                  60
Glu Ser Arg Ile Arg Arg Pro Met Asn Ala Phe Met Val Trp Ala Lys
65                  70                  75                  80
Asp Glu Arg Lys Arg Leu Ala Gln Gln Asn Pro Asp Leu His Asn Ala
                85                  90                  95
Glu Leu Ser Lys Met Leu Gly Lys Ser Trp Lys Ala Leu Thr Leu Ala
            100                 105                 110
Glu Lys Arg Pro Phe Val Glu Glu Ala Glu Arg Leu Arg Val Gln His
        115                 120                 125
Met Gln Asp His Pro Asn Tyr Lys Tyr Arg Pro Arg Arg Arg Lys Gln
    130                 135                 140
Val Lys Arg Leu Lys Arg Val Glu Gly Gly Phe Leu His Gly Leu Ala
145                 150                 155                 160
Glu Pro Gln Ala Ala Ala Leu Gly Pro Glu Gly Gly Arg Val Ala Met
                165                 170                 175
Asp Gly Leu Gly Leu Gln Phe Pro Glu Gln Gly Phe Pro Ala Gly Pro
            180                 185                 190
Pro Leu Leu Pro Pro His Met Gly Gly His Tyr Arg Asp Cys Gln Ser
        195                 200                 205
Leu Gly Ala Pro Pro Leu Asp Gly Tyr Pro Leu Pro Thr Pro Asp Thr
    210                 215                 220
Ser Pro Leu Asp Gly Val Asp Pro Asp Pro Ala Phe Phe Ala Ala Pro
225                 230                 235                 240
Met Pro Gly Asp Cys Pro Ala Ala Gly Thr Tyr Ser Tyr Ala Gln Val
                245                 250                 255
Ser Asp Tyr Ala Gly Pro Pro Glu Pro Pro Ala Gly Pro Met His Pro
            260                 265                 270
Arg Leu Gly Pro Glu Pro Ala Gly Pro Ser Ile Pro Gly Leu Leu Ala
        275                 280                 285
Pro Pro Ser Ala Leu His Val Tyr Tyr Gly Ala Met Gly Ser Pro Gly
    290                 295                 300
Ala Gly Gly Gly Arg Gly Phe Gln Met Gln Pro Gln His Gln His Gln
305                 310                 315                 320
His Gln His Gln His His Pro Pro Gly Pro Gly Gln Pro Ser Pro Pro
                325                 330                 335
Pro Glu Ala Leu Pro Cys Arg Asp Gly Thr Asp Pro Ser Gln Pro Ala
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                340                 345                 350
Glu Leu Leu Gly Glu Val Asp Arg Thr Glu Phe Glu Gln Tyr Leu His
            355                 360                 365
Phe Val Cys Lys Pro Glu Met Gly Leu Pro Tyr Gln Gly His Asp Ser
        370                 375                 380
Gly Val Asn Leu Pro Asp Ser His Gly Ala Ile Ser Ser Val Val Ser
385                 390                 395                 400
Asp Ala Ser Ser Ala Val Tyr Tyr Cys Asn Tyr Pro Asp Val
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<210> 104
<211> 2398
<212> DNA
<213> Homo sapiens

<400> 104

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<210> 105
<211> 232
<212> PRT
<213> Homo sapiens

<400> 105
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Ser Ala Val Gln Cys Ile Ala Asn Pro Ile Lys Leu Ala Arg Leu Val
            20   25   30
Met Glu Lys Thr Pro His Cys Phe Leu Thr Asp Gln Gly Ala Ala Gln
        35   40   45
Phe Ala Ala Ala Met Gly Val Pro Glu Ile Pro Gly Glu Lys Leu Val
    50   55   60
Thr Glu Arg Asn Lys Lys Arg Leu Glu Lys Glu Lys His Glu Lys Gly
65   70   75   80
Ala Gln Lys Thr Asp Cys Gln Lys Asn Leu Gly Thr Val Gly Ala Val
                85   90   95
Ala Leu Asp Cys Lys Gly Asn Val Ala Tyr Ala Thr Ser Thr Gly Gly
            100   105   110
Ile Val Asn Lys Met Val Gly Arg Val Gly Asp Ser Pro Cys Leu Gly
        115   120   125
Ala Gly Gly Tyr Ala Asp Asn Asp Ile Gly Ala Val Ser Thr Thr Gly
    130   135   140
His Gly Glu Ser Ile Leu Lys Val Asn Leu Ala Arg Leu Thr Leu Phe
145   150   155   160
His Ile Glu Gln Gly Lys Thr Val Glu Glu Ala Ala Asp Leu Ser Leu
                165   170   175
Gly Tyr Met Lys Ser Arg Val Lys Gly Leu Gly Gly Leu Ile Val Val
            180   185   190
Ser Lys Thr Gly Asp Trp Val Ala Lys Trp Thr Ser Thr Ser Met Pro
        195   200   205
Trp Ala Ala Ala Lys Asp Gly Lys Leu His Phe Gly Ile Asp Pro Asp
    210   215   220
Asp Thr Thr Ile Thr Asp Leu Pro
225   230

<210> 106
<211> 1811
<212> DNA
<213> Homo sapiens

<400> 106
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cacagtcact actgtcgcct cagctgggaa cattggggag gatggaatcc agagctgcac 240
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cagaggccgg acagcagtgt ttgctgatca agtgatagtt ggcaatgcct ctttgcggct 420
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cagctttgag ctgaactctg agaatgtgac catgaaggtt gtgtctgtgc tctacaatgt 720
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tatcaaagtg acagaatcgg agatcaaaag gcggagtcac ctacagctgc taaactcaaa 840

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<210> 107
<211> 282
<212> PRT
<213> Homo sapiens

<400> 107

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Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
            20                  25                  30
Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
        35                  40                  45
Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
    50                  55                  60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65                  70                  75                  80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
                85                  90                  95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
            100                 105                 110
Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
        115                 120                 125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
    130                 135                 140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
145                 150                 155                 160
Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
                165                 170                 175
Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
            180                 185                 190
Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
        195                 200                 205
Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
    210                 215                 220
Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225                 230                 235                 240
Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
                245                 250                 255
Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
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Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys
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<210> 108
<211> 2611
<212> DNA
<213> Homo sapiens

<400> 108
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cagatggcca tggtgaagtg tggacagact ggaataatat gtccaagttt ttccagtatg 180
gatggcgatg caccactaat gagaatacct attcaaaccg taccctgatg ggcaactgga 240
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gacactactt tgaaacaaca tatgatacaa gctacaacaa caaaatgcca ctttcaacac 360
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atgataagat acttcacttt tccagagtga aatgtaggag ggagcacatt ctaagtacag 600
ctaaaaattt agctcactgt aacacagttt cactctctga ataaataaag caaaaaacac 660
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<210> 109
<211> 150
<212> PRT

<213> Homo sapiens

<400> 109

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Gln Asn Leu Ala Cys Phe Leu Thr Asn Pro His Cys Gly Ser Leu Val
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Asn Ala Asp Gly His Gly Glu Val Trp Thr Asp Trp Asn Asn Met Ser
35 40 45
Lys Phe Phe Gln Tyr Gly Trp Arg Cys Thr Thr Asn Glu Asn Thr Tyr
50 55 60
Ser Asn Arg Thr Leu Met Gly Asn Trp Asn Gln Glu Arg Tyr Asp Leu
65 70 75 80
Arg Asn Ile Val Gln Pro Lys Pro Leu Pro Ser Gln Phe Gly His Tyr
85 90 95
Phe Glu Thr Thr Tyr Asp Thr Ser Tyr Asn Asn Lys Met Pro Leu Ser
100 105 110
Thr His Arg Phe Lys Arg Glu Pro His Trp Phe Pro Gly His Gln Pro
115 120 125
Glu Leu Asp Pro Pro Arg Tyr Lys Cys Thr Glu Lys Ser Thr Tyr Met
130 135 140
Asn Ser Tyr Ser Lys Pro
145 150

<210> 110
<211> 1032
<212> DNA
<213> Homo sapiens

<400> 110

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ggccctcaag ggacagacat ggctcagcgg atgacaacac agctgctgct ccttctagtg 180
tgggtggctg tagtagggga ggctcagaca aggattgcat gggccaggac tgagcttctc 240
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aaccagacac cg 1032

<210> 111
<211> 257
<212> PRT
<213> Homo sapiens

<400> 111

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Leu Leu Asn Val Cys Met Asn Ala Lys His His Lys Glu Lys Pro Gly
        35                  40                  45
Pro Glu Asp Lys Leu His Glu Gln Cys Arg Pro Trp Arg Lys Asn Ala
    50                  55                  60
Cys Cys Ser Thr Asn Thr Ser Gln Glu Ala His Lys Asp Val Ser Tyr
65                  70                  75                  80
Leu Tyr Arg Phe Asn Trp Asn His Cys Gly Glu Met Ala Pro Ala Cys
                85                  90                  95
Lys Arg His Phe Ile Gln Asp Thr Cys Leu Tyr Glu Cys Ser Pro Asn
            100                 105                 110
Leu Gly Pro Trp Ile Gln Gln Val Asp Gln Ser Trp Arg Lys Glu Arg
        115                 120                 125
Val Leu Asn Val Pro Leu Cys Lys Glu Asp Cys Glu Gln Trp Trp Glu
    130                 135                 140
Asp Cys Arg Thr Ser Tyr Thr Cys Lys Ser Asn Trp His Lys Gly Trp
145                 150                 155                 160
Asn Trp Thr Ser Gly Phe Asn Lys Cys Ala Val Gly Ala Ala Cys Gln
                165                 170                 175
Pro Phe His Phe Tyr Phe Pro Thr Pro Thr Val Leu Cys Asn Glu Ile
            180                 185                 190
Trp Thr His Ser Tyr Lys Val Ser Asn Tyr Ser Arg Gly Ser Gly Arg
        195                 200                 205
Cys Ile Gln Met Trp Phe Asp Pro Ala Gln Gly Asn Pro Asn Glu Glu
    210                 215                 220
Val Ala Arg Phe Tyr Ala Ala Ala Met Ser Gly Ala Gly Pro Trp Ala
225                 230                 235                 240
Ala Trp Pro Phe Leu Leu Ser Leu Ala Leu Met Leu Leu Trp Leu Leu
                245                 250                 255
Ser
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<210> 112
<211> 1104
<212> DNA
<213> Homo sapiens

<400> 112

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<210> 113
<211> 939
<212> DNA
<213> Homo sapiens

<400> 113
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attgcatggg ccaggactga gcttctcaat gtctgcatga acgccaagca ccacaaggaa 180
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tggaaccact gtggagagat ggcacctgcc tgcaaacggc atttcatcca ggacacctgc 360
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<210> 114
<211> 1331
<212> DNA
<213> Homo sapiens

<400> 114
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<210> 115
<211> 929
<212> DNA

<213> Homo sapiens

<400> 115
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catgaacgcc aagcaccaca aggaaaagcc aggccccgag gacaagttgc atgagcagtg 180
tcgaccctgg aggaagaatg cctgctgttc taccaacacc agccaggaag cccataagga 240
tgtttcctac ctatatagat tcaactggaa ccactgtgga gagatggcac ctgcctgcaa 300
acggcatttc atccaggaca cctgcctcta cgagtgctcc cccaacttgg ggccctggat 360
ccagcaggtg gatcagagct ggcgcaaaga gcgggtactg aacgtgcccc tgtgcaaaga 420
ggactgtgag caatggtggg aagattgtcg cacctcctac acctgcaaga gcaactggca 480
caagggctgg aactggactt cagggtttaa caagtgcgca gtgggagctg cctgccaacc 540
tttccatttc tacttcccca cacccactgt tctgtgcaat gaaatctgga ctcactccta 600
caaggtcagc aactacagcc gagggagtgg ccgctgcatc cagatgtggt tcgacccagc 660
ccagggcaac cccaatgagg aggtggcgag gttctatgct gcagccatga gtggggctgg 720
gccctgggca gcctggcctt tcctgcttag cctggcccta atgctgctgt ggctgctcag 780
ctgacctcct tttaccttct gatacctgga aatccctgcc ctgttcagcc ccacagctcc 840
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accgcacatg tgtcttgaga attatttgg 929

<210> 116
<211> 858
<212> DNA
<213> Homo sapiens

<400> 116
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ccaggagtgc gcgggccagg acggacctgc tcaatgtctg catgaacgcc aagcaccaca 180
agacacagcc cagccccgag gacgagctgt atggccagtg cagtccctgg aagaagaatg 240
cctgctgcac ggccagcacc agccaggagc tgcacaagga cacctcccgc ctgtacaact 300
ttaactggga tcactgtggt aagatggaac ccacctgcaa gcgccacttt atccaggaca 360
gctgtctcta tgagtgctca cccaacctgg ggccctggat ccggcaggtc aaccagagct 420
ggcgcaaaga gcgcattctg aacgtgcccc tgtgcaaaga ggactgtgag cgctggtggg 480
aggactgtcg cacctcctac acctgcaaaa gcaactggca caaaggctgg aattggacct 540
cagggattaa tgagtgtccg gccggggccc tctgcagcac ctttgagtcc tacttcccca 600
ctccagccgc cctttgtgaa ggcctctgga gccactcctt caaggtcagc aactatagtc 660
gagggagcgg ccgctgcatc cagatgtggt ttgactcagc ccagggcaac cccaatgagg 720
aggtggccaa gttctatgct gcggccatga atgctggggc cccgtctcgt gggattattg 780
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ccacatgaaa aaaaaaaa 858

<210> 117
<211> 243
<212> PRT
<213> Homo sapiens

<400> 117
Met Ala Trp Gln Met Met Gln Leu Leu Leu Leu Ala Leu Val Thr Ala
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Ala Gly Ser Ala Gln Pro Arg Ser Ala Arg Ala Arg Thr Asp Leu Leu
20 25 30
Asn Val Cys Met Asn Ala Lys His His Lys Thr Gln Pro Ser Pro Glu
35 40 45
Asp Glu Leu Tyr Gly Gln Cys Ser Pro Trp Lys Lys Asn Ala Cys Cys
50 55 60
Thr Ala Ser Thr Ser Gln Glu Leu His Lys Asp Thr Ser Arg Leu Tyr
65 70 75 80

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Asn Phe Asn Trp Asp His Cys Gly Lys Met Glu Pro Thr Cys Lys Arg
                85                  90                  95
His Phe Ile Gln Asp Ser Cys Leu Tyr Glu Cys Ser Pro Asn Leu Gly
            100                 105                 110
Pro Trp Ile Arg Gln Val Asn Gln Ser Trp Arg Lys Glu Arg Ile Leu
        115                 120                 125
Asn Val Pro Leu Cys Lys Glu Asp Cys Glu Arg Trp Trp Glu Asp Cys
    130                 135                 140
Arg Thr Ser Tyr Thr Cys Lys Ser Asn Trp His Lys Gly Trp Asn Trp
145                 150                 155                 160
Thr Ser Gly Ile Asn Glu Cys Pro Ala Gly Ala Leu Cys Ser Thr Phe
                165                 170                 175
Glu Ser Tyr Phe Pro Thr Pro Ala Ala Leu Cys Glu Gly Leu Trp Ser
            180                 185                 190
His Ser Phe Lys Val Ser Asn Tyr Ser Arg Gly Ser Gly Arg Cys Ile
        195                 200                 205
Gln Met Trp Phe Asp Ser Ala Gln Gly Asn Pro Asn Glu Glu Val Ala
    210                 215                 220
Lys Phe Tyr Ala Ala Ala Met Asn Ala Gly Ala Pro Ser Arg Gly Ile
225                 230                 235                 240
Ile Asp Ser
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<210> 118
<211> 1362
<212> DNA
<213> Homo sapiens

<400> 118

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ttcgtgatgg gccttctggg gaacagcgcc accattcggg tcacccaggt gctgcagaag 180
aaaggatact tgcagaagga ggtgacagac cacatggtga gtttggcttg ctcggacatc 240
ttggtgttcc tcatcggcat gcccatggag ttctacagca tcatctggaa tcccctgacc 300
acgtccagct acaccctgtc ctgcaagctg cacactttcc tcttcgaggc ctgcagctac 360
gctacgctgc tgcacgtgct gacactcagc tttgagcgct acatcgccat ctgtcacccc 420
ttcaggtaca aggctgtgtc gggaccttgc caggtgaagc tgctgattgg cttcgtctgg 480
gtcacctccg ccctggtggc actgcccttg ctgtttgcca tgggtactga gtacccccctg 540
gtgaacgtgc ccagccaccg gggtctcact tgcaaccgct ccagcacccg ccaccacgag 600
cagcccgaga cctccaatat gtccatctgt accaacctct ccagccgctg gaccgtgttc 660
cagtccagca tcttcggcgc cttcgtggtc tacctcgtgg tcctgctctc cgtagccttc 720
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acgcggcctc cgcagctgag gaagtccgag agcgaagaga gcaggaccgc caggaggcag 840
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tgccgcctgt cgctgcagca cgccaaccac gagaagcgcc tgcgcgtaca tgcgcactcc 1140
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tctgcaagga gaactgagaa gatttctta agcacttttc agagcgaggc cgagccccag 1260
tctaagtccc agtcattgag tctcgagtca ctagagccca actcaggcgc gaaaccagcc 1320
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<210> 119
<211> 453
<212> PRT
<213> Homo sapiens

<400> 119

Met Ala Ser Pro Ser Leu Pro Gly Ser Asp Cys Ser Gln Ile Ile Asp
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His Ser His Val Pro Glu Phe Glu Val Ala Thr Trp Ile Lys Ile Thr
20 25 30
Leu Ile Leu Val Tyr Leu Ile Ile Phe Val Met Gly Leu Leu Gly Asn
35 40 45
Ser Ala Thr Ile Arg Val Thr Gln Val Leu Gln Lys Lys Gly Tyr Leu
50 55 60
Gln Lys Glu Val Thr Asp His Met Val Ser Leu Ala Cys Ser Asp Ile
65 70 75 80
Leu Val Phe Leu Ile Gly Met Pro Met Glu Phe Tyr Ser Ile Ile Trp
85 90 95
Asn Pro Leu Thr Thr Ser Ser Tyr Thr Leu Ser Cys Lys Leu His Thr
100 105 110
Phe Leu Phe Glu Ala Cys Ser Tyr Ala Thr Leu Leu His Val Leu Thr
115 120 125
Leu Ser Phe Glu Arg Tyr Ile Ala Ile Cys His Pro Phe Arg Tyr Lys
130 135 140
Ala Val Ser Gly Pro Cys Gln Val Lys Leu Leu Ile Gly Phe Val Trp
145 150 155 160
Val Thr Ser Ala Leu Val Ala Leu Pro Leu Leu Phe Ala Met Gly Thr
165 170 175
Glu Tyr Pro Leu Val Asn Val Pro Ser His Arg Gly Leu Thr Cys Asn
180 185 190
Arg Ser Ser Thr Arg His His Glu Gln Pro Glu Thr Ser Asn Met Ser
195 200 205
Ile Cys Thr Asn Leu Ser Ser Arg Trp Thr Val Phe Gln Ser Ser Ile
210 215 220
Phe Gly Ala Phe Val Val Tyr Leu Val Val Leu Leu Ser Val Ala Phe
225 230 235 240
Met Cys Trp Asn Met Met Gln Val Leu Met Lys Ser Gln Lys Gly Ser
245 250 255
Leu Ala Gly Gly Thr Arg Pro Pro Gln Leu Arg Lys Ser Glu Ser Glu
260 265 270
Glu Ser Arg Thr Ala Arg Arg Gln Thr Ile Ile Phe Leu Arg Leu Ile
275 280 285
Val Val Thr Leu Ala Val Cys Trp Met Pro Asn Gln Ile Arg Arg Ile
290 295 300
Met Ala Ala Ala Lys Pro Lys His Asp Trp Thr Arg Ser Tyr Phe Arg
305 310 315 320
Ala Tyr Met Ile Leu Leu Pro Phe Ser Glu Thr Phe Phe Tyr Leu Ser
325 330 335
Ser Val Ile Asn Pro Leu Leu Tyr Thr Val Ser Ser Gln Gln Phe Arg
340 345 350
Arg Val Phe Val Gln Val Leu Cys Cys Arg Leu Ser Leu Gln His Ala
355 360 365
Asn His Glu Lys Arg Leu Arg Val His Ala His Ser Thr Thr Asp Ser
370 375 380
Ala Arg Phe Val Gln Arg Pro Leu Leu Phe Ala Ser Arg Arg Gln Ser
385 390 395 400
Ser Ala Arg Arg Thr Glu Lys Ile Phe Leu Ser Thr Phe Gln Ser Glu
405 410 415
Ala Glu Pro Gln Ser Lys Ser Gln Ser Leu Ser Leu Glu Ser Leu Glu
420 425 430
Pro Asn Ser Gly Ala Lys Pro Ala Asn Ser Ala Ala Glu Asn Gly Phe
435 440 445

Gln Glu His Glu Val
    450

<210> 120
<211> 2870
<212> DNA
<213> Homo sapiens

<400> 120
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tcagagagaa agatgagagc tcaccaggtg ctcaccttcc tcctgctctt cgtgatcacc 180
tcggtggcct ctgaaaacgc cagcacatcc cgaggctgtg ggctggacct cctccctcag 240
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gcgggcgccc tgatcacact gctcctgatg ctcatcctcc tggtgcggct gcccttcatc 360
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ggcctctttg ggctgacgtt tgccttcatc atccaggagg acgagaccat ctgctctgtc 480
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<210> 121
<211> 403
<212> PRT
<213> Homo sapiens

<400> 121
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            20                  25                  30
Thr Ser Arg Gly Cys Gly Leu Asp Leu Leu Pro Gln Tyr Val Ser Leu
        35                  40                  45
Cys Asp Leu Asp Ala Ile Trp Gly Ile Val Val Glu Ala Val Ala Gly
    50                  55                  60
Ala Gly Ala Leu Ile Thr Leu Leu Leu Met Leu Ile Leu Leu Val Arg
65                  70                  75                  80
Leu Pro Phe Ile Lys Glu Lys Glu Lys Lys Ser Pro Val Gly Leu His
                85                  90                  95
Phe Leu Phe Leu Leu Gly Thr Leu Gly Leu Phe Gly Leu Thr Phe Ala
            100                 105                 110
Phe Ile Ile Gln Glu Asp Glu Thr Ile Cys Ser Val Arg Arg Phe Leu
        115                 120                 125
Trp Gly Val Leu Phe Ala Leu Cys Phe Ser Cys Leu Leu Ser Gln Ala
    130                 135                 140
Trp Arg Val Arg Arg Leu Val Arg His Gly Thr Gly Pro Ala Gly Trp
145                 150                 155                 160
Gln Leu Val Gly Leu Ala Leu Cys Leu Met Leu Val Gln Val Ile Ile
                165                 170                 175
Ala Val Glu Trp Leu Val Leu Thr Val Leu Arg Asp Thr Arg Pro Ala
            180                 185                 190
Cys Ala Tyr Glu Pro Met Asp Phe Val Met Ala Leu Ile Tyr Asp Met
        195                 200                 205
Val Leu Leu Val Val Thr Leu Gly Leu Ala Leu Phe Thr Leu Cys Gly
    210                 215                 220
Lys Phe Lys Arg Trp Lys Leu Asn Gly Ala Phe Leu Leu Ile Thr Ala
225                 230                 235                 240
Phe Leu Ser Val Leu Ile Trp Val Ala Trp Met Thr Met Tyr Leu Phe
                245                 250                 255
Gly Asn Val Lys Leu Gln Gln Gly Asp Ala Trp Asn Asp Pro Thr Leu
            260                 265                 270
Ala Ile Thr Leu Ala Ala Ser Gly Trp Val Phe Val Ile Phe His Ala
        275                 280                 285
Ile Pro Glu Ile His Cys Thr Leu Leu Pro Ala Leu Gln Glu Asn Thr
    290                 295                 300
Pro Asn Tyr Phe Asp Thr Ser Gln Pro Arg Met Arg Glu Thr Ala Phe
305                 310                 315                 320
Glu Glu Asp Val Gln Leu Pro Arg Ala Tyr Met Glu Asn Lys Ala Phe
                325                 330                 335
Ser Met Asp Glu His Asn Ala Ala Leu Arg Thr Ala Gly Phe Pro Asn
            340                 345                 350
Gly Ser Leu Gly Lys Arg Pro Ser Gly Ser Leu Gly Lys Arg Pro Ser
        355                 360                 365
Ala Pro Phe Arg Ser Asn Val Tyr Gln Pro Thr Glu Met Ala Val Val
    370                 375                 380
Leu Asn Gly Gly Thr Ile Pro Thr Ala Pro Pro Ser His Thr Gly Arg
385                 390                 395                 400
His Leu Trp
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<210> 122
<211> 1474
<212> DNA
<213> Homo sapiens

<400> 122
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agtctcctca tatgtgcaag ctcggccctc ccctggaatc taaagcctcc tcagccttct 180
gagtcagcct gaaaggaaca ggccgaactg ctgtatgggc tctactgcca gtgtgacctc 240
accctctcca gtcacccctc ctcagttcca gctatgagtt cctgcaactt cacacatgcc 300
acctgtgtgc ttattggtat cccaggatta gagaaagccc atttctgggt tggcttcccc 360
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gagattagca ttgaggcctg tcttacccag atgttcttta ttcatgccct ctcagccatt 600
gaatccacca tcctgctggc catggccttt gaccgttatg tggccatctg ccacccactg 660
cgccatgctg cagtgctcaa caatacagta acagcccaga ttggcatcgt ggctgtggtc 720
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tgtgacaagg acttgcaggc tgtgggaggc aagtgaccct taacactaca cttctcctta 1260
tctttattgg cttgataaac ataattattt ctaacactag cttatttcca gttgcccata 1320
agcacatcag tacttttctc tggctggaat agtaaactaa agtatggtac atctacctaa 1380
aggactatta tgtggaataa tacatactaa tgaagtatta catgatttaa agactacaat 1440
aaaaccaaac atgcttataa cattaaaaaa aaaa 1474

<210> 123
<211> 320
<212> PRT
<213> Homo sapiens

<400> 123
Met Ser Ser Cys Asn Phe Thr His Ala Thr Cys Val Leu Ile Gly Ile
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Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser
20 25 30
Met Tyr Val Val Ala Met Cys Gly Asn Cys Ile Val Val Phe Ile Val
35 40 45
Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
50 55 60
Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
65 70 75 80
Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Ile Glu Ala Cys
85 90 95
Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
100 105 110
Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
115 120 125
Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly

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    130                 135                 140
Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
145                 150                 155                 160
Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
                165                 170                 175
Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
            180                 185                 190
Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
        195                 200                 205
Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
    210                 215                 220
Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
225                 230                 235                 240
Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
                245                 250                 255
Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
            260                 265                 270
Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
        275                 280                 285
Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
    290                 295                 300
Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys
305                 310                 315                 320
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<210> 124
<211> 2205
<212> DNA
<213> Homo sapiens

<400> 124
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gccagacttc ggaacgggtg tcctgctact cctgctgggg ctcctccagg acaagggcac 180
acaactggtt ccgttaagcc cctctctcgc tcagacgcca tggagctgga tctgtctcca 240
cctcatctta gcagctctcc ggaagacctt tggccagccc ctgggacccc tcctgggact 300
ccccggcccc ctgatacccc tctgcctgag gaggtaaaga ggtcccagcc tctcctcatc 360
ccaaccaccg gcaggaaact tcgagaggag gagaggcgtg ccacctccct cccctctatc 420
cccaacccct tccctgagct ctgcagtcct ccctcacaga gcccaattct cgggggcccc 480
tccagtgcaa gggggctgct cccccgcgat gccagccgcc cccatgtagt aaaggtgtac 540
agtgaggatg gggcctgcag gtctgtggag gtggcagcag gtgccacagc tcgccacgtg 600
tgtgaaatgc tggtgcagcg agctcacgcc ttgagcgacg agacctgggg gctggtggag 660
tgccaccccc acctagcact ggagcggggt ttggaggacc acgagtccgt ggtggaagtg 720
caggctgcct ggcccgtggg cggagatagc cgcttcgtct tccggaaaaa cttcgccaag 780
tacgaactgt tcaagagctc cccacactcc ctgttcccag aaaaaatggt ctccagctgt 840
ctcgatgcac acactggtat atcccatgaa gacctcatcc agaacttcct gaatgctggc 900
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gatccgaggc acctgcagta cgtggcagat gtgaacgagt ccaacgtgta cgtggtgacg 1080
cagggccgca agctctacgg gatgcccact gacttcggtt tctgtgtcaa gcccaacaag 1140
cttcgaaatg gacacaaggg gcttcggatc ttctgcagtg aagatgagca gagccgcacc 1200
tgctggctgg ctgccttccg cctcttcaag tacggggtgc agctgtacaa gaattaccag 1260
caggcacagt ctcgccatct gcatccatct tgtttgggct ccccacccct gagaagtgcc 1320
tcagataata ccctggtggc catggacttc tctggccatg ctgggcgtgt cattgagaac 1380
ccccgggagg ctctgagtgt ggccctggag gaggcccagg cctggaggaa gaagacaaac 1440
caccgcctca gcctgcccat gccagcctcc ggcacgagcc tcagtgcagc catccaccgc 1500
acccaactct ggttccacgg gcgcatttcc cgtgaggaga gccagcggct tattggacag 1560
cagggcttgg tagacggcct gttcctggtc cgggagagtc agcggaaccc ccagggcttt 1620
```

gtcctctctt tgtgccacct gcagaaagtg aagcattatc tcatcctgcc gagcgaggag 1680
gagggtcgcc tgtacttcag catggatgat ggccagaccc gcttcactga cctgctgcag 1740
ctcgtggagt tccaccagct gaaccgcggc atcctgccgt gcttgctgcg ccattgctgc 1800
acgcgggtgg ccctctgacc aggccgtgga ctggctcatg cctcagcccg ccttcaggct 1860
gcccgccgcc cctccaccca tccagtggac tctgggcgc ggccacaggg gacgggatga 1920
ggagcgggag ggttccgcca ctccagtttt ctcctctgct tctttgcctc cctcagatag 1980
aaaacagccc ccactccagt ccactcctga cccctctcct caagggaagg ccttgggtgg 2040
ccccctctcc ttctcctagc tctggaggtg ctgctctagg gcagggaatt atgggagaag 2100
tgggggcagc ccaggcggtt tcacgcccca cactttgtac agaccgagag gccagttgat 2160
ctgctctgtt ttatactagt gacaataaag attatttttt gatac 2205

<210> 125
<211> 532
<212> PRT
<213> Homo sapiens

<400> 125
Met Glu Leu Asp Leu Ser Pro Pro His Leu Ser Ser Ser Pro Glu Asp
1 5 10 15
Leu Trp Pro Ala Pro Gly Thr Pro Pro Gly Thr Pro Arg Pro Pro Asp
20 25 30
Thr Pro Leu Pro Glu Glu Val Lys Arg Ser Gln Pro Leu Leu Ile Pro
35 40 45
Thr Thr Gly Arg Lys Leu Arg Glu Glu Glu Arg Arg Ala Thr Ser Leu
50 55 60
Pro Ser Ile Pro Asn Pro Phe Pro Glu Leu Cys Ser Pro Pro Ser Gln
65 70 75 80
Ser Pro Ile Leu Gly Gly Pro Ser Ser Ala Arg Gly Leu Leu Pro Arg
85 90 95
Asp Ala Ser Arg Pro His Val Val Lys Val Tyr Ser Glu Asp Gly Ala
100 105 110
Cys Arg Ser Val Glu Val Ala Ala Gly Ala Thr Ala Arg His Val Cys
115 120 125
Glu Met Leu Val Gln Arg Ala His Ala Leu Ser Asp Glu Thr Trp Gly
130 135 140
Leu Val Glu Cys His Pro His Leu Ala Leu Glu Arg Gly Leu Glu Asp
145 150 155 160
His Glu Ser Val Val Glu Val Gln Ala Ala Trp Pro Val Gly Gly Asp
165 170 175
Ser Arg Phe Val Phe Arg Lys Asn Phe Ala Lys Tyr Glu Leu Phe Lys
180 185 190
Ser Ser Pro His Ser Leu Phe Pro Glu Lys Met Val Ser Ser Cys Leu
195 200 205
Asp Ala His Thr Gly Ile Ser His Glu Asp Leu Ile Gln Asn Phe Leu
210 215 220
Asn Ala Gly Ser Phe Pro Glu Ile Gln Gly Phe Leu Gln Leu Arg Gly
225 230 235 240
Ser Gly Arg Lys Leu Trp Lys Arg Phe Phe Cys Phe Leu Arg Arg Ser
245 250 255
Gly Leu Tyr Tyr Ser Thr Lys Gly Thr Ser Lys Asp Pro Arg His Leu
260 265 270
Gln Tyr Val Ala Asp Val Asn Glu Ser Asn Val Tyr Val Val Thr Gln
275 280 285
Gly Arg Lys Leu Tyr Gly Met Pro Thr Asp Phe Gly Phe Cys Val Lys
290 295 300
Pro Asn Lys Leu Arg Asn Gly His Lys Gly Leu Arg Ile Phe Cys Ser
305 310 315 320
Glu Asp Glu Gln Ser Arg Thr Cys Trp Leu Ala Ala Phe Arg Leu Phe

```
                    325                 330                 335
Lys Tyr Gly Val Gln Leu Tyr Lys Asn Tyr Gln Gln Ala Gln Ser Arg
            340                 345                 350
His Leu His Pro Ser Cys Leu Gly Ser Pro Pro Leu Arg Ser Ala Ser
        355                 360                 365
Asp Asn Thr Leu Val Ala Met Asp Phe Ser Gly His Ala Gly Arg Val
    370                 375                 380
Ile Glu Asn Pro Arg Glu Ala Leu Ser Val Ala Leu Glu Glu Ala Gln
385                 390                 395                 400
Ala Trp Arg Lys Lys Thr Asn His Arg Leu Ser Leu Pro Met Pro Ala
                405                 410                 415
Ser Gly Thr Ser Leu Ser Ala Ala Ile His Arg Thr Gln Leu Trp Phe
            420                 425                 430
His Gly Arg Ile Ser Arg Glu Glu Ser Gln Arg Leu Ile Gly Gln Gln
        435                 440                 445
Gly Leu Val Asp Gly Leu Phe Leu Val Arg Glu Ser Gln Arg Asn Pro
    450                 455                 460
Gln Gly Phe Val Leu Ser Leu Cys His Leu Gln Lys Val Lys His Tyr
465                 470                 475                 480
Leu Ile Leu Pro Ser Glu Glu Glu Gly Arg Leu Tyr Phe Ser Met Asp
                485                 490                 495
Asp Gly Gln Thr Arg Phe Thr Asp Leu Leu Gln Leu Val Glu Phe His
            500                 505                 510
Gln Leu Asn Arg Gly Ile Leu Pro Cys Leu Leu Arg His Cys Cys Thr
        515                 520                 525
Arg Val Ala Leu
    530
```

<210> 126
<211> 1619
<212> DNA
<213> Homo sapiens

<400> 126

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agttctgcgg tgccagggag tggagcagag ctcagccccg tcccaaacac agatgggacc 60
atgaactccg gacacagctt cagccagacc ccctcggcct ccttccatgg cgccggaggt 120
ggctggggcc ggcccaggag cttccccagg gctcccaccg tccatggcgg tgcgggggga 180
gcccgcatct ccctgtcctt caccacgcgg agctgcccac cccctggagg gtcttggggt 240
tctggaagaa gcagccccct actaggcgga aatgggaagg ccaccatgca gaatctcaac 300
gaccgcctgg cctcctacct ggagaaggtt cgcgccctgg aggaggccaa catgaagctg 360
gaaagccgca tcctgaaatg gcaccagcag agagatcctg gcagtaagaa agattattcc 420
cagtatgagg aaaacatcac acacctgcag gagcagatag tggatggtaa gatgaccaat 480
gctcagatta ttcttctcat tgacaatgcc aggatggcag tggatgactt caacctcaag 540
tatgaaaatg aacactcctt taagaaagac ttggaaattg aagtcgaggg cctccgaagg 600
accttagaca acctgaccat tgtcacaaca gacctagaac aggaggtgga aggaatgagg 660
aaagagctca ttctcatgaa ggagcaccat gagcaggaaa tggaggagca tcatgtgcca 720
agtgacttca atgtcaatgt gaaggtggat acaggtccca gggaagatct gattaaggtc 780
ctggaggata tgagacaaga atatgagctt ataataaaga agaagcatcg agacttggac 840
acttggtata aagaacagtc tgcagccatg tcccaggagg cagccagtcc agccactgtg 900
cagagcagac aaggtgacat ccacgaactg aagcgcacat tccaggccct ggagattgac 960
ctgcaggcac agtacagcac gaaatctgct ttggaaaaca tgttatccga gacccagtct 1020
cggtactcct gcaagctcca ggacatgcaa gagatcatct cccactatga ggaggaactg 1080
acgcagctac gccacgaact ggagcggcag aacaatgaat accaagtgct gctgggcatc 1140
aaaacccacc tggagaagga aatcaccacg taccgacggc tcctggaggg agagagtgaa 1200
gggacacggg aagaatcaaa gtcgagcatg aaagtgtctg caactccaaa gatcaaggcc 1260
ataacccagg agaccatcaa cggaagatta gttctttgtc aagtgaatga aatccaaaag 1320
cacgcatgag accaatgaaa gtttccgcct gttgtaaagt ctattttccc ccaaggaaag 1380
```

tccttgcaca gacaccagtg agtgagttct aaaagatacc cttggaatta tcagactcag 1440
aaacttttat tttttttttt ctgtaacagt ctcaccagac ttctcataat gctcttaata 1500
tattgcactt ttctaatcaa agtgcgagtt tatgagggta aagctctact ttcctactgc 1560
agccttcaga ttctcatcat tttgcatcta ttttgtagcc aataaaactc cgcactagc 1619

<210> 127
<211> 422
<212> PRT
<213> Homo sapiens

<400> 127
Met Asn Ser Gly His Ser Phe Ser Gln Thr Pro Ser Ala Ser Phe His
1 5 10 15
Gly Ala Gly Gly Gly Trp Gly Arg Pro Arg Ser Phe Pro Arg Ala Pro
20 25 30
Thr Val His Gly Gly Ala Gly Gly Ala Arg Ile Ser Leu Ser Phe Thr
35 40 45
Thr Arg Ser Cys Pro Pro Pro Gly Gly Ser Trp Gly Ser Gly Arg Ser
50 55 60
Ser Pro Leu Leu Gly Gly Asn Gly Lys Ala Thr Met Gln Asn Leu Asn
65 70 75 80
Asp Arg Leu Ala Ser Tyr Leu Glu Lys Val Arg Ala Leu Glu Glu Ala
85 90 95
Asn Met Lys Leu Glu Ser Arg Ile Leu Lys Trp His Gln Gln Arg Asp
100 105 110
Pro Gly Ser Lys Lys Asp Tyr Ser Gln Tyr Glu Glu Asn Ile Thr His
115 120 125
Leu Gln Glu Gln Ile Val Asp Gly Lys Met Thr Asn Ala Gln Ile Ile
130 135 140
Leu Leu Ile Asp Asn Ala Arg Met Ala Val Asp Asp Phe Asn Leu Lys
145 150 155 160
Tyr Glu Asn Glu His Ser Phe Lys Lys Asp Leu Glu Ile Glu Val Glu
165 170 175
Gly Leu Arg Arg Thr Leu Asp Asn Leu Thr Ile Val Thr Thr Asp Leu
180 185 190
Glu Gln Glu Val Glu Gly Met Arg Lys Glu Leu Ile Leu Met Lys Glu
195 200 205
His His Glu Gln Glu Met Glu Glu His His Val Pro Ser Asp Phe Asn
210 215 220
Val Asn Val Lys Val Asp Thr Gly Pro Arg Glu Asp Leu Ile Lys Val
225 230 235 240
Leu Glu Asp Met Arg Gln Glu Tyr Glu Leu Ile Ile Lys Lys Lys His
245 250 255
Arg Asp Leu Asp Thr Trp Tyr Lys Glu Gln Ser Ala Ala Met Ser Gln
260 265 270
Glu Ala Ala Ser Pro Ala Thr Val Gln Ser Arg Gln Gly Asp Ile His
275 280 285
Glu Leu Lys Arg Thr Phe Gln Ala Leu Glu Ile Asp Leu Gln Ala Gln
290 295 300
Tyr Ser Thr Lys Ser Ala Leu Glu Asn Met Leu Ser Glu Thr Gln Ser
305 310 315 320
Arg Tyr Ser Cys Lys Leu Gln Asp Met Gln Glu Ile Ile Ser His Tyr
325 330 335
Glu Glu Glu Leu Thr Gln Leu Arg His Glu Leu Glu Arg Gln Asn Asn
340 345 350
Glu Tyr Gln Val Leu Leu Gly Ile Lys Thr His Leu Glu Lys Glu Ile
355 360 365
Thr Thr Tyr Arg Arg Leu Leu Glu Gly Glu Ser Glu Gly Thr Arg Glu

```
    370                 375                 380
Glu Ser Lys Ser Ser Met Lys Val Ser Ala Thr Pro Lys Ile Lys Ala
385                 390                 395                 400
Ile Thr Gln Glu Thr Ile Asn Gly Arg Leu Val Leu Cys Gln Val Asn
                405                 410                 415
Glu Ile Gln Lys His Ala
            420
```

<210> 128
<211> 1359
<212> DNA
<213> Homo sapiens

<400> 128

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cttttggtg taaatctgga ctctaattct gtaatatatc aaggaatctc gtaaaaccga 60
cactaaaacg tccctgccta caaatcatcc ggccaaatta tgagttcatt gtattatgcg 120
aatgctttat tttctaaata tccagcctca agttcggttt tcgctaccgg agccttccca 180
gaacaaactt cttgtgcgtt tgcttccaac ccccagcgcc cgggctatgg agcgggttcg 240
ggcgcttcct tcgccggctc gatgcagggc ttgtaccccg gcgggggggg catggcgggc 300
cagagcgcgg ccggcgtcta cgcggccggc tatgggctcg agccgagttc cttcaacatg 360
cactgcgcgc cctttgagca gaacctctcc ggggtgtgtc ccggcgactc cgccaaggcg 420
gcgggcgcca aggagcagag ggactcggac ttggcggccg agagtaactt ccggatctac 480
ccctcgatgc gaagctcagg aactgaccgc aaacgaggcc gccagaccta cacccgctac 540
cagaccctgg agctggagaa ggaatttcac tacaatcgct acctgacgcg gcggcggcgc 600
atcgagatcg cgcacgcgct ctgcctcacg gaaagacaga tcaagatttg gtttcagaac 660
cggcgcatga agtggaaaaa ggagaacaag accgcgggcc cggggaccac cggccaagac 720
agggctgaag cagaggagga agaggaagag tgagggatgg agaaagggca gaggaagaga 780
catgagaaag ggagacgaag agaagcccag ctctgggaac tgaatcagga aactcaaatc 840
gaatagggaa gtaaaaaaac aaaacaaaaa acaaaaaaaa acaaaaaaaa accctattta 900
aatgaaagga gtttaaaaac atttttaag gagggagaaa ggagaaattt tggtttttca 960
acactgaaaa aatagtacct ataggaaagt ctgtcaggtt tggtttttt gtacaatatg 1020
aaaaggacat tatctacctg ttctgtagct ttctggaatt tacctcccct tttctatgtt 1080
gctattgtaa ggtctttgta aaatcttgca gttttgtaag ccctctttaa tgctgtcttt 1140
gtggactgtg ggtctggact aaccctgtgg ttgcctgccc tcctgtgcct ccgccttccc 1200
agcagcggca ccaaggggcc ttagggagcc ccaaaaccta ccactcgcgt gttccccaag 1260
cgccttgctg ctgctgcttg cttcccgtcc cccagcccca tgctcccttt acattctgtg 1320
tgtatctaaa ggatggaaaa ataaaacgca attaaaaat                        1359
```

<210> 129
<211> 217
<212> PRT
<213> Homo sapiens

<400> 129

```
Met Ser Ser Leu Tyr Tyr Ala Asn Ala Leu Phe Ser Lys Tyr Pro Ala
 1               5                  10                  15
Ser Ser Ser Val Phe Ala Thr Gly Ala Phe Pro Glu Gln Thr Ser Cys
            20                  25                  30
Ala Phe Ala Ser Asn Pro Gln Arg Pro Gly Tyr Gly Ala Gly Ser Gly
        35                  40                  45
Ala Ser Phe Ala Gly Ser Met Gln Gly Leu Tyr Pro Gly Gly Gly Gly
    50                  55                  60
Met Ala Gly Gln Ser Ala Ala Gly Val Tyr Ala Ala Gly Tyr Gly Leu
65                  70                  75                  80
Glu Pro Ser Ser Phe Asn Met His Cys Ala Pro Phe Glu Gln Asn Leu
                85                  90                  95
Ser Gly Val Cys Pro Gly Asp Ser Ala Lys Ala Ala Gly Ala Lys Glu
```

```
            100                 105                 110
Gln Arg Asp Ser Asp Leu Ala Ala Glu Ser Asn Phe Arg Ile Tyr Pro
        115                 120                 125
Ser Met Arg Ser Ser Gly Thr Asp Arg Lys Arg Gly Arg Gln Thr Tyr
    130                 135                 140
Thr Arg Tyr Gln Thr Leu Glu Leu Glu Lys Glu Phe His Tyr Asn Arg
145                 150                 155                 160
Tyr Leu Thr Arg Arg Arg Arg Ile Glu Ile Ala His Ala Leu Cys Leu
                165                 170                 175
Thr Glu Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp
            180                 185                 190
Lys Lys Glu Asn Lys Thr Ala Gly Pro Gly Thr Thr Gly Gln Asp Arg
        195                 200                 205
Ala Glu Ala Glu Glu Glu Glu Glu Glu
    210                 215
```

<210> 130
<211> 1257
<212> DNA
<213> Homo sapiens

<400> 130

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gaggcgcgcg ggtgaaaggc gcattgatgc agcctgcggc ggcctcggag cgcggcggag 60
cagacgctga ccacgttcct ctcctcggtc tcctccgcct ccagctccgc gctgcccggc 120
agccgggagc catgcgaccc cagggccccg ccgcctcccc gcagcggctc cgcggcctcc 180
tgctgctcct gctgctgcag ctgcccgcgc cgtcgagcgc ctctgagatc cccaagggga 240
agcaaaaggc gcagctccgg cagagggagg tggtggacct gtataatgga atgtgcttac 300
aagggccagc aggagtgcct ggtcgagacg ggagccctgg ggccaatggc attccgggta 360
cacctgggat cccaggtcgg gatggattca aaggagaaaa gggggaatgt ctgagggaaa 420
gctttgagga gtcctggaca cccaactaca agcagtgttc atggagttca ttgaattatg 480
gcatagatct tgggaaaatt gcggagtgta catttacaaa gatgcgttca aatagtgctc 540
taagagtttt gttcagtggc tcacttcggc taaaatgcag aaatgcatgc tgtcagcgtt 600
ggtatttcac attcaatgga gctgaatgtt caggacctct tcccattgaa gctataattt 660
atttggacca aggaagccct gaaatgaatt caacaattaa tattcatcgc acttcttctg 720
tggaaggact ttgtgaagga attggtgctg gattagtgga tgttgctatc tgggttggca 780
cttgttcaga ttacccaaaa ggagatgctt ctactggatg gaattcagtt tctcgcatca 840
ttattgaaga actaccaaaa taaatgcttt aattttcatt tgctacctct ttttttatta 900
tgccttggaa tggttcactt aaatgacatt ttaaataagt ttatgtatac atctgaatga 960
aaagcaaagc taaatatgtt tacagaccaa agtgtgattt cacactgttt ttaaatctag 1020
cattattcat tttgcttcaa tcaaaagtgg tttcaatatt ttttttagtt ggttagaata 1080
ctttcttcat agtcacattc tctcaaccta taatttggaa tattgttgtg gtcttttgtt 1140
ttttctctta gtatagcatt ttttaaaaaaa tataaaagct accaatcttt gtacaatttg 1200
taaatgttaa gaattttttt tatatctgtt aaataaaaat tatttccaac aacctta    1257
```

<210> 131
<211> 278
<212> PRT
<213> Homo sapiens

<400> 131

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Met Gln Pro Ala Ala Ala Ser Glu Arg Gly Gly Ala Asp Ala Asp His
1               5                   10                  15
Val Pro Leu Leu Gly Leu Leu Arg Leu Gln Leu Arg Ala Ala Arg Gln
            20                  25                  30
Pro Gly Ala Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu
        35                  40                  45
Arg Gly Leu Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser
```

```
    50                  55                  60
Ala Ser Glu Ile Pro Lys Gly Lys Gln Lys Ala Gln Leu Arg Gln Arg
65                  70                  75                  80
Glu Val Val Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly
                85                  90                  95
Val Pro Gly Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr
            100                 105                 110
Pro Gly Ile Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys
        115                 120                 125
Leu Arg Glu Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys
    130                 135                 140
Ser Trp Ser Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu
145                 150                 155                 160
Cys Thr Phe Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe
                165                 170                 175
Ser Gly Ser Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp
            180                 185                 190
Tyr Phe Thr Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu
        195                 200                 205
Ala Ile Ile Tyr Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile
    210                 215                 220
Asn Ile His Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly
225                 230                 235                 240
Ala Gly Leu Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr
                245                 250                 255
Pro Lys Gly Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile
            260                 265                 270
Ile Glu Glu Leu Pro Lys
        275
```

<210> 132
<211> 1177
<212> DNA
<213> Homo sapiens

<400> 132

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cacgcgtccg aatttacttt gttggacaac cacagctggg gctaggaatg gttcagaagg 60
tttaaggccg gaaagggaaa tgaaggggcc cggcgctaac cctctaagga cctgttttgc 120
ttctgtttaa accaaatggg cagtctgtca ttacacacac cctgggtctt catatgtggc 180
cgccagtata atggaatgtg cttacaaggg ccagcaggag tgcctggtcg agacgggagc 240
cctggggcca atggcattcc gggtacacct gggatcccag gtcgggatgg attcaaagga 300
gaaaaggggg aatgtctgag ggaaagcttt gaggagtcct ggacacccaa ctacaagcag 360
tgttcatgga gttcattgaa ttatggcata gatcttggga aaattgcgga gtgtacattt 420
acaaagatgc gttcaaatag tgctctaaga gttttgttca gtggctcact tcggctaaaa 480
tgcagaaatg catgctgtca gcgttggtat ttcacattca atggagctga atgttcagga 540
cctcttccca ttgaagctat aatttatttg gaccaaggaa gccctgaaat gaattcaaca 600
attaatattc atcgcacttc ttctgtggaa ggactttgtg aaggaattgg tgctggatta 660
gtggatgttg ctatctgggt tggcacttgt tcagattacc caaaaggaga tgcttctact 720
ggatggaatt cagtttctcg catcattatt gaagaactac caaaataaat gctttaattt 780
tcatttgcta cctctttttt tattatgcct tggaatggtt cacttaaatg acattttaaa 840
taagtttatg tatacatctg aatgaaaagc aaagctaaat atgtttacag accaaagtgt 900
gatttcacac tgtttttaaa tctagcatta ttcattttgc ttcaatcaaa agtggtttca 960
atattttttt tagttggtta gaatactttc ttcatagtca cattctctca acctataatt 1020
tggaatattg ttgtggtctt ttgttttttc tcttagtata gcatttttaa aaaaatataa 1080
aagctaccaa tctttgtaca atttgtaaat gttaagaatt ttttttatat ctgttaaata 1140
aaaattattt ccaacaaccw waaaaaaaaa aaaaagg                         1177
```

<210> 133
<211> 210
<212> PRT
<213> Homo sapiens

<400> 133
Met Gly Ser Leu Ser Leu His Thr Pro Trp Val Phe Ile Cys Gly Arg
1 5 10 15
Gln Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro Gly Arg
20 25 30
Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile Pro
35 40 45
Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg Glu Ser
50 55 60
Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp Ser Ser
65 70 75 80
Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr Phe Thr
85 90 95
Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly Ser Leu
100 105 110
Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe Thr Phe
115 120 125
Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile Tyr
130 135 140
Leu Asp Gln Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His Arg
145 150 155 160
Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu Val
165 170 175
Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly Asp
180 185 190
Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu Leu
195 200 205
Pro Lys
210

<210> 134
<211> 1340
<212> DNA
<213> Homo sapiens

<400> 134
agggagtcga cccacgcgtc cggaagctcc gggtgtcgcg ggggcgggag gaattaaggg 60
agggagagag gcgcgcgggt gaaaggcgca ttgatgcagc ctgcggcggc ctcggagcgc 120
ggcggagcca gacgctgacc acgttcctct cctcggtctc ctccgcctcc agctccgcgc 180
tgcccggcag ccgggagcca tgcgacccca gggccccgcc gcctccccgc agcggctccg 240
cggcctcctg ctgctcctgc tgctgcagct gcccgcgccg tcgagcgcct ctgagatccc 300
caaggggaag caaaaggcgc agctccggca gagggaggtg gtggacctgt ataatggaat 360
gtgcttacaa gggccagcag gagtgcctgg tcgagacggg agccctgggg ccaatggcat 420
tccgggtaca cctgggatcc caggtcggga tggattcaaa ggagaaaagg gggaatgtct 480
gagggaaagc tttgaggagt cctggacacc caactacaag cagtgttcat ggagttcatt 540
gaattatggc atagatcttg ggaaaattgc ggagtgtaca tttacaaaga tgcgttcaaa 600
tagtgctcta agagttttgt tcagtggctc acttcggcta aaatgcagaa atgcatgctg 660
tcagcgttgg tatttcacat tcaatggagc tgaatgttca ggacctcttc ccattgaagc 720
tataatttat ttggaccaag gaagccctga aatgaattca acaattaata ttcatcgcac 780
ttcttctgtg gaaggacttt gtgaaggaat tggtgctgga ttagtggatg ttgctatctg 840
ggttggcact tgttcagatt acccaaaagg agatgcttct actggatgga attcagtttc 900
tcgcatcatt attgaagaac taccaaaata aatgctttaa ttttcatttg ctacctcttt 960

ttttattatg ccttggaatg gttcacttaa atgacatttt aaataagttt atgtatacat 1020
ctgaatgaaa agcaaagcta aatatgttta cagaccaaag tgtgatttca cactgttttt 1080
aaatctagca ttattcattt tgcttcaatc aaaagtggtt tcaatatttt ttttagttgg 1140
ttagaatact ttcttcatag tcacattctc tcaacctata atttggaata ttgttgtggt 1200
cttttgtttt ttctcttagt atagcatttt taaaaaaata taaaagctac caatctttgt 1260
acaatttgta aatgttaaga atttttttta tatctgttaa ataaaaatta tttccaacaa 1320
ccwwaaaaaa aaaaaaaagg 1340

<210> 135
<211> 243
<212> PRT
<213> Homo sapiens

<400> 135
Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu Arg Gly Leu
1 5 10 15
Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser Ala Ser Glu
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Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu
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<211> 5519
<212> DNA
<213> Homo sapiens

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<210> 137
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<212> PRT
<213> *Homo sapiens*

<400> 137

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Lys Thr Lys Leu Asp Thr Leu Ala Thr Gly His Leu Phe Gln Glu Val
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Arg Cys Met Lys Leu Val Gln His Pro Asn Ile Val Arg Leu Tyr Glu
65                  70                  75                  80
Val Ile Asp Thr Gln Thr Lys Leu Tyr Leu Ile Leu Glu Leu Gly Asp
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Glu Asp Leu Pro Lys Lys Tyr Phe Ala Gln Ile Val His Ala Ile Ser
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Tyr Cys His Lys Leu His Val Val His Arg Asp Leu Lys Pro Glu Asn
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Val Val Phe Phe Glu Lys Gln Gly Leu Val Lys Leu Thr Asp Phe Gly
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Val Cys Gly Gln Pro Pro Phe Gln Glu Ala Asn Asp Ser Glu Thr Leu
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Thr Met Ile Met Asp Cys Lys Tyr Thr Val Pro Ser His Val Ser Lys
225 230 235 240
Glu Cys Lys Asp Leu Ile Thr Arg Met Leu Gln Arg Asp Pro Lys Arg
245 250 255
Arg Ala Ser Leu Glu Glu Ile Glu Asn His Pro Trp Leu Gln Gly Val
260 265 270
Asp Pro Ser Pro Ala Thr Lys Tyr Asn Ile Pro Leu Val Ser Tyr Lys
275 280 285
Asn Leu Ser Glu Glu Glu His Asn Ser Ile Ile Gln Arg Met Val Leu
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Val Asp Lys Ala Ser Pro Ser Glu Asn Asn Ala Gly Gly Gly Ser Pro
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        675                 680                 685
Ile Ser Ser Thr Gly Asn Ala Gly Gln Val Pro Ala Val Gly Gly Ile
    690                 695                 700
Lys Phe Phe Ser Asp His Met Ala Asp Thr Thr Thr Glu Leu Glu Arg
705                 710                 715                 720
Ile Lys Ser Lys Asn Leu Lys Asn Asn Val Leu Gln Leu Pro Leu Cys
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<210> 138
<211> 2029
<212> DNA
<213> Homo sapiens

<400> 138

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<211> 379
<212> PRT
<213> Homo sapiens

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Leu Glu Gly Leu Gly Leu Asn Leu Gln Lys Ser Ser Glu Lys Glu Leu
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Asp Leu Gln Asp Thr Phe Val Ser Ala Met Lys Thr Leu Tyr Leu Ala
115 120 125
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130 135 140
Ile Asn Asp Tyr Val Ala Lys Gln Thr Lys Gly Lys Ile Val Asp Leu
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Leu Lys Asn Leu Asp Ser Asn Ala Val Val Ile Met Val Asn Tyr Ile
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Phe Phe Lys Ala Lys Trp Glu Thr Ser Phe Asn His Lys Gly Thr Gln
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Ala Ala Thr Gly Thr Ile Phe Thr Phe Arg Ser Ala Arg Leu Asn Ser
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<212> DNA
<213> Homo sapiens

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tgtgagttct ttgagaaaca gcgtggattt tacttatctg tgtattcaca gagcttagca 1920
cagtgcctgg taatgagcaa gcatacttgc cattactttt ccttcccact ctctccaaca 1980
tcacattcac tttaaatttt tctgtatata gaaaggaaaa ctagcctggg caacatgatg 2040
aaaccccatc tccactgc 2058

<210> 141
<211> 413
<212> PRT
<213> Homo sapiens

<400> 141
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1 5 10 15
Ile Asp Tyr Asn Met Ile Val Ala Phe Met Leu Gly Asn Tyr Ile Asn
20 25 30
Leu Arg Glu Ser Ser Thr Glu Pro Asn Asp Ser Leu Trp Phe Ser Leu
35 40 45
Gln Lys Lys Asn Asp Thr Thr Glu Ile Glu Thr Leu Leu Leu Asn Thr
50 55 60
Ala Pro Lys Ile Ile Asp Glu Gln Leu Val Cys Arg Leu Ser Lys Thr
65 70 75 80

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Asp Ile Phe Ile Ile Cys Arg Asp Asn Lys Ile Tyr Leu Asp Lys Met
                85                  90                  95
Ile Thr Arg Asn Leu Lys Leu Arg Phe Tyr Gly His Arg Gln Tyr Leu
            100                 105                 110
Glu Cys Glu Val Phe Arg Val Glu Gly Ile Lys Asp Asn Leu Asp Asp
        115                 120                 125
Ile Lys Arg Ile Ile Lys Ala Arg Glu His Arg Asn Arg Leu Leu Ala
    130                 135                 140
Asp Ile Arg Asp Tyr Arg Pro Tyr Ala Asp Leu Val Ser Glu Ile Arg
145                 150                 155                 160
Ile Leu Leu Val Gly Pro Val Gly Ser Gly Lys Ser Ser Phe Phe Asn
                165                 170                 175
Ser Val Lys Ser Ile Phe His Gly His Val Thr Gly Gln Ala Val Val
            180                 185                 190
Gly Ser Asp Thr Thr Ser Ile Thr Glu Arg Tyr Arg Ile Tyr Ser Val
        195                 200                 205
Lys Asp Gly Lys Asn Gly Lys Ser Leu Pro Phe Met Leu Cys Asp Thr
    210                 215                 220
Met Gly Leu Asp Gly Ala Glu Gly Ala Gly Leu Cys Met Asp Asp Ile
225                 230                 235                 240
Pro His Ile Leu Lys Gly Cys Met Pro Asp Arg Tyr Gln Phe Asn Ser
                245                 250                 255
Arg Lys Pro Ile Thr Pro Glu His Ser Thr Phe Ile Thr Ser Pro Ser
            260                 265                 270
Leu Lys Asp Arg Ile His Cys Val Ala Tyr Val Leu Asp Ile Asn Ser
        275                 280                 285
Ile Asp Asn Leu Tyr Ser Lys Met Leu Ala Lys Val Lys Gln Val His
    290                 295                 300
Lys Glu Val Leu Asn Cys Gly Ile Ala Tyr Val Ala Leu Leu Thr Lys
305                 310                 315                 320
Val Asp Asp Cys Ser Glu Val Leu Gln Asp Asn Phe Leu Asn Met Ser
                325                 330                 335
Arg Ser Met Thr Ser Gln Ser Arg Val Met Asn Val His Lys Met Leu
            340                 345                 350
Gly Ile Pro Ile Ser Asn Ile Leu Met Val Gly Asn Tyr Ala Ser Asp
        355                 360                 365
Leu Glu Leu Asp Pro Met Lys Asp Ile Leu Ile Leu Ser Ala Leu Arg
    370                 375                 380
Gln Met Leu Arg Ala Ala Asp Asp Phe Leu Glu Asp Leu Pro Leu Glu
385                 390                 395                 400
Glu Thr Gly Ala Ile Glu Arg Ala Leu Gln Pro Cys Ile
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<210> 142
<211> 1032
<212> DNA
<213> Homo sapiens

<400> 142

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gctggacgtc cccacggcgg cggtgcaggc gtcccctctg caagcgttag acttctttgg 180
gaatgggcca ccagttaact acaagacagg caatctatac ctgcgggggc ccctgaagaa 240
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agccttcctg atccgggagc tcttcccaac atggctgttg gtcatggaga tcctcaatgt 360
cacgtcggtg ccctacggaa acgcacagga acaaaatgtc agtggcaggt gggagttcaa 420
gtgccagctt ggagaagagg agtgcaaatt caacaaggtg gaggcctgcg tgttggatga 480
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tcatggagtg tgcaatgggg gaccgcggca tgcagctcat gcacgccaac gcccagcgga 660
cagatgctct ccagccaccg cacgagtatg tgccctgggt caccgtcaat gggaaaccct 720
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gctgcggaga gctcatggaa ggcgagtggg aactcggctg cctgcctttt tttctgatcc 900
agaccctcgg cacctgctac ttaccaactg gaaaatttta tgcatcccat gaagcccaga 960
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aactagttta at 1032

<210> 143
<211> 303
<212> PRT
<213> Homo sapiens

<400> 143
Met Asp Ser Arg His Thr Phe Ala Pro Ala Ala Met Thr Leu Ser Pro
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Leu Leu Leu Phe Leu Pro Pro Leu Leu Leu Leu Leu Asp Val Pro Thr
20 25 30
Ala Ala Val Gln Ala Ser Pro Leu Gln Ala Leu Asp Phe Phe Gly Asn
35 40 45
Gly Pro Pro Val Asn Tyr Lys Thr Gly Asn Leu Tyr Leu Arg Gly Pro
50 55 60
Leu Lys Lys Ser Asn Ala Pro Leu Val Asn Val Thr Leu Tyr Tyr Glu
65 70 75 80
Ala Leu Cys Gly Gly Cys Arg Ala Phe Leu Ile Arg Glu Leu Phe Pro
85 90 95
Thr Trp Leu Leu Val Met Glu Ile Leu Asn Val Thr Ser Val Pro Tyr
100 105 110
Gly Asn Ala Gln Glu Gln Asn Val Ser Gly Arg Trp Glu Phe Lys Cys
115 120 125
Gln Leu Gly Glu Glu Glu Cys Lys Phe Asn Lys Val Glu Ala Cys Val
130 135 140
Leu Asp Glu Leu Asp Met Glu Leu Ala Phe Leu Thr Met Ser Gly Met
145 150 155 160
Ala Trp Lys Ser Leu Arg Thr Trp Arg Glu Val Cys His Tyr Ala Cys
165 170 175
Ser Ser Thr Pro Gln Gly Cys Arg Gln Asn Tyr His Gly Val Cys Asn
180 185 190
Gly Gly Pro Arg His Ala Ala His Ala Arg Gln Arg Pro Ala Asp Arg
195 200 205
Cys Ser Pro Ala Thr Ala Arg Val Cys Ala Leu Gly His Arg Gln Trp
210 215 220
Glu Thr Leu Gly Arg Ser Asp Pro Ala Pro Tyr Pro Cys Leu Pro Val
225 230 235 240
Val Pro Gly Gln Glu Ala Gly Cys Leu Pro Phe Leu Asn Gln Leu Pro
245 250 255
Pro Glu Cys Leu Leu Arg Val Leu Ala Gly Gly Leu Arg Arg Ala His
260 265 270
Gly Arg Arg Val Gly Thr Arg Leu Pro Ala Phe Phe Ser Asp Pro Asp
275 280 285
Pro Arg His Leu Leu Leu Thr Asn Trp Lys Ile Leu Cys Ile Pro
290 295 300

<210> 144

<211> 1356
<212> DNA
<213> Homo sapiens

<400> 144
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ttctgtttct ctccgtgctg ttctctcccg ctgtgcgcct gcccgcctct cgctgtcctc 180
tctccccctc gccctctctt cggccccccc ctttcacgtt cactctgtct ctcccactat 240
ctctgccccc ctctatcctt gatacaacag ctgacctcat ttcccgatac cttttccccc 300
ccgaaaagta caacatctgg cccgccccag cccgaagaca gcccgtcctc cctggacaat 360
cagacgaatt ctcccccccc ccccaaaaaa aaaagccatc cccccgctct gccccgtcgc 420
acattcggcc cccgcgactc ggccagagcg gcgctggcag aggagtgtcc ggcaggaggg 480
ccaacgcccg ctgttcggtt tgcgacacgc agcagggagg tgggcggcag cgtcgccggc 540
ttccagacac caatgggaat cccaatgggg aagtcgatgc tggtgcttct caccttcttg 600
gccttcgcct cgtgctgcat tgctgcttac cgccccagtg agaccctgtg cggcggggag 660
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ccccctgggg cttctcctga cccagtcccc gtgccccgcc tccccgaaac aggctactct 1260
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<210> 145
<211> 180
<212> PRT
<213> Homo sapiens

<400> 145
Met Gly Ile Pro Met Gly Lys Ser Met Leu Val Leu Leu Thr Phe Leu
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Ala Phe Ala Ser Cys Cys Ile Ala Ala Tyr Arg Pro Ser Glu Thr Leu
20 25 30
Cys Gly Gly Glu Leu Val Asp Thr Leu Gln Phe Val Cys Gly Asp Arg
35 40 45
Gly Phe Tyr Phe Ser Arg Pro Ala Ser Arg Val Ser Arg Arg Ser Arg
50 55 60
Gly Ile Val Glu Glu Cys Cys Phe Arg Ser Cys Asp Leu Ala Leu Leu
65 70 75 80
Glu Thr Tyr Cys Ala Thr Pro Ala Lys Ser Glu Arg Asp Val Ser Thr
85 90 95
Pro Pro Thr Val Leu Pro Asp Asn Phe Pro Arg Tyr Pro Val Gly Lys
100 105 110
Phe Phe Gln Tyr Asp Thr Trp Lys Gln Ser Thr Gln Arg Leu Arg Arg
115 120 125
Gly Leu Pro Ala Leu Leu Arg Ala Arg Arg Gly His Val Leu Ala Lys
130 135 140
Glu Leu Glu Ala Phe Arg Glu Ala Lys Arg His Arg Pro Leu Ile Ala
145 150 155 160
Leu Pro Thr Gln Asp Pro Ala His Gly Gly Ala Pro Pro Glu Met Ala
165 170 175
Ser Asn Arg Lys

180

<210> 146
<211> 3667
<212> DNA
<213> Homo sapiens

<400> 146
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aaatatgagg gaagtttatt gtgttcttac tttaaatagt ttgcagtttt attgtgtata 180
caaatgtatg catgtgaaat atacagattt taaaaaagca gatcattaaa gattaggtca 240
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tcgaagctag cctggatttg aatcttggat ccaccactga ctagctatgt aagcttagtc 360
aagcaactca acggaggagg cgaggagcgc cgggtaccgg gccgggggag ccgcgggctc 420
tcggggaaga gacggatgat gaacaagctt tacatcggga acctgagccc cgccgtcacc 480
gccgacgacc tccggcagct ctttggggac aggaagctgc ccctggcggg acaggtcctg 540
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gagaccctct cgggtaaagt ggaattgcat gggaaaatca tggaagttga ttactcagtc 660
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<210> 147
<211> 556
<212> PRT
<213> Homo sapiens

<400> 147

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Met Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Pro Ala Val Thr Ala
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Asp Asp Leu Arg Gln Leu Phe Gly Asp Arg Lys Leu Pro Leu Ala Gly
            20                  25                  30
Gln Val Leu Leu Lys Ser Gly Tyr Ala Phe Val Asp Tyr Pro Asp Gln
        35                  40                  45
Asn Trp Ala Ile Arg Ala Ile Glu Thr Leu Ser Gly Lys Val Glu Leu
    50                  55                  60
His Gly Lys Ile Met Glu Val Asp Tyr Ser Val Ser Lys Lys Leu Arg
65                  70                  75                  80
Ser Arg Lys Ile Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu
                85                  90                  95
Val Leu Asp Gly Leu Leu Ala Gln Tyr Gly Thr Val Glu Asn Val Glu
            100                 105                 110
Gln Val Asn Thr Asp Thr Glu Thr Ala Val Val Asn Val Thr Tyr Ala
        115                 120                 125
Thr Arg Glu Glu Ala Lys Ile Ala Met Glu Lys Leu Ser Gly His Gln
    130                 135                 140
Phe Glu Asn Tyr Ser Phe Lys Ile Ser Tyr Ile Pro Asp Glu Glu Val
145                 150                 155                 160
Ser Ser Pro Ser Pro Pro Gln Arg Ala Gln Arg Gly Asp His Ser Ser
                165                 170                 175
Arg Glu Gln Gly His Ala Pro Gly Gly Thr Ser Gln Ala Arg Gln Ile
            180                 185                 190
Asp Phe Pro Leu Arg Ile Leu Val Pro Thr Gln Phe Val Gly Ala Ile
        195                 200                 205
Ile Gly Lys Glu Gly Leu Thr Ile Lys Asn Ile Thr Lys Gln Thr Gln
    210                 215                 220
Ser Arg Val Asp Ile His Arg Lys Glu Asn Ser Gly Ala Ala Glu Lys
225                 230                 235                 240
Pro Val Thr Ile His Ala Thr Pro Glu Gly Thr Ser Glu Ala Cys Arg
                245                 250                 255
Met Ile Leu Glu Ile Met Gln Lys Glu Ala Asp Glu Thr Lys Leu Ala
            260                 265                 270
Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Gly Leu Val Gly Arg
        275                 280                 285
Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu His Glu Thr
    290                 295                 300
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Gly Thr Lys Ile Thr Ile Ser Ser Leu Gln Asp Leu Ser Ile Tyr Asn
305                 310                 315                 320
Pro Glu Arg Thr Ile Thr Val Lys Gly Thr Val Glu Ala Cys Ala Ser
                325                 330                 335
Ala Glu Ile Glu Ile Met Lys Lys Leu Arg Glu Ala Phe Glu Asn Asp
            340                 345                 350
Met Leu Ala Val Asn Thr His Ser Gly Tyr Phe Ser Ser Leu Tyr Pro
        355                 360                 365
His His Gln Phe Gly Pro Phe Pro His His His Ser Tyr Pro Glu Gln
    370                 375                 380
Glu Ile Val Asn Leu Phe Ile Pro Thr Gln Ala Val Gly Ala Ile Ile
385                 390                 395                 400
Gly Lys Lys Gly Ala His Ile Lys Gln Leu Ala Arg Phe Ala Gly Ala
                405                 410                 415
Ser Ile Lys Ile Ala Pro Ala Glu Gly Pro Asp Val Ser Glu Arg Met
            420                 425                 430
Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe Lys Ala Gln Gly Arg
        435                 440                 445
Ile Phe Gly Lys Leu Lys Glu Glu Asn Phe Phe Asn Pro Lys Glu Glu
    450                 455                 460
Val Lys Leu Glu Ala His Ile Arg Val Pro Ser Ser Thr Ala Gly Arg
465                 470                 475                 480
Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu Leu Gln Asn Leu Thr
                485                 490                 495
Ser Ala Glu Val Ile Val Pro Arg Asp Gln Thr Pro Asp Glu Asn Glu
            500                 505                 510
Glu Val Ile Val Arg Ile Ile Gly His Phe Phe Ala Ser Gln Thr Ala
        515                 520                 525
Gln Arg Lys Ile Arg Glu Ile Val Gln Gln Val Lys Gln Gln Glu Gln
    530                 535                 540
Lys Tyr Pro Gln Gly Val Ala Ser Gln Arg Ser Lys
545                 550                 555
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<210> 148
<211> 1475
<212> DNA
<213> Homo sapiens

<400> 148

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ccagcttcga gaaagagttg agaagttaaa catgctcagc attgatcatc tcacagacca 240
caagtcacag cgccttgcac gtctagttct gggatgcatc accatggcat atgtgtgggg 300
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atttcgtgat ggagactgca gtaaaggatt cttcctggtc tctctattgg tggaaatagc 540
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ggacactttg ctaaaggcgc tgttggaaat agcttcttgc ttggagaaag cccttcaagt 660
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tacaactgag aaatcccttt tgaaggaagg ttaatgtaac ccaacaagag cacattttat 1260
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cttgtaggaa aacaacaaaa ggtaattatg tgtaattata ctagaagttt tgtaatctgt 1440
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<210> 149
<211> 403
<212> PRT
<213> Homo sapiens

<400> 149
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Ile Asp Glu Glu Val Gly Phe Ala Leu Pro Asn Pro Gln Glu Asn Leu
20 25 30
Pro Asp Phe Tyr Asn Asp Trp Met Phe Ile Ala Lys His Leu Pro Asp
35 40 45
Leu Ile Glu Ser Gly Gln Leu Arg Glu Arg Val Glu Lys Leu Asn Met
50 55 60
Leu Ser Ile Asp His Leu Thr Asp His Lys Ser Gln Arg Leu Ala Arg
65 70 75 80
Leu Val Leu Gly Cys Ile Thr Met Ala Tyr Val Trp Gly Lys Gly His
85 90 95
Gly Asp Val Arg Lys Val Leu Pro Arg Asn Ile Ala Val Pro Tyr Cys
100 105 110
Gln Leu Ser Lys Lys Leu Glu Leu Pro Pro Ile Leu Val Tyr Ala Asp
115 120 125
Cys Val Leu Ala Asn Trp Lys Lys Lys Asp Pro Asn Lys Pro Leu Thr
130 135 140
Tyr Glu Asn Met Asp Val Leu Phe Ser Phe Arg Asp Gly Asp Cys Ser
145 150 155 160
Lys Gly Phe Phe Leu Val Ser Leu Leu Val Glu Ile Ala Ala Ala Ser
165 170 175
Ala Ile Lys Val Ile Pro Thr Val Phe Lys Ala Met Gln Met Gln Glu
180 185 190
Arg Asp Thr Leu Leu Lys Ala Leu Leu Glu Ile Ala Ser Cys Leu Glu
195 200 205
Lys Ala Leu Gln Val Phe His Gln Ile His Asp His Val Asn Pro Lys
210 215 220
Ala Phe Phe Ser Val Leu Arg Ile Tyr Leu Ser Gly Trp Lys Gly Asn
225 230 235 240
Pro Gln Leu Ser Asp Gly Leu Val Tyr Glu Gly Phe Trp Glu Asp Pro
245 250 255
Lys Glu Phe Ala Gly Gly Ser Ala Gly Gln Ser Ser Val Phe Gln Cys
260 265 270
Phe Asp Val Leu Leu Gly Ile Gln Gln Thr Ala Gly Gly Gly His Ala
275 280 285
Ala Gln Phe Leu Gln Asp Met Arg Arg Tyr Met Pro Pro Ala His Arg
290 295 300
Asn Phe Leu Cys Ser Leu Glu Ser Asn Pro Ser Val Arg Glu Phe Val
305 310 315 320
Leu Ser Lys Gly Asp Ala Gly Leu Arg Glu Ala Tyr Asp Ala Cys Val
325 330 335
Lys Ala Leu Val Ser Leu Arg Ser Tyr His Leu Gln Ile Val Thr Lys
340 345 350

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Tyr Ile Leu Ile Pro Ala Ser Gln Gln Pro Lys Glu Asn Lys Thr Ser
        355                 360                 365
Glu Asp Pro Ser Lys Leu Glu Ala Lys Gly Thr Gly Gly Thr Asp Leu
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<210> 150
<211> 2129
<212> DNA
<213> Homo sapiens

<400> 150

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<210> 151
<211> 465
<212> PRT
<213> Homo sapiens

<400> 151

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Gly Thr Ser Thr Leu Ala Leu Gln Leu Gly Gln Arg Leu Gly Gly Glu
35 40 45
Ile Val Ser Ala Asp Ser Met Gln Val Tyr Glu Gly Leu Asp Ile Ile
50 55 60
Thr Asn Lys Val Ser Ala Gln Glu Gln Arg Ile Cys Arg His His Met
65 70 75 80
Ile Ser Phe Val Asp Pro Leu Val Thr Asn Tyr Thr Val Val Asp Phe
85 90 95
Arg Asn Arg Ala Thr Ala Leu Ile Glu Asp Ile Phe Ala Arg Asp Lys
100 105 110
Ile Pro Ile Val Val Gly Gly Thr Asn Tyr Tyr Ile Glu Ser Leu Leu
115 120 125
Trp Lys Val Leu Val Asn Thr Lys Pro Gln Glu Met Gly Thr Glu Lys
130 135 140
Val Ile Asp Arg Lys Val Glu Leu Glu Lys Glu Asp Gly Leu Val Leu
145 150 155 160
His Lys Arg Leu Ser Gln Val Asp Pro Glu Met Ala Ala Lys Leu His
165 170 175
Pro His Asp Lys Arg Lys Val Ala Arg Ser Leu Gln Val Phe Glu Glu
180 185 190
Thr Gly Ile Ser His Ser Glu Phe Leu His Arg Gln His Thr Glu Glu
195 200 205
Gly Gly Gly Pro Leu Gly Gly Pro Leu Lys Phe Ser Asn Pro Cys Ile
210 215 220
Leu Trp Leu His Ala Asp Gln Ala Val Leu Asp Glu Arg Leu Asp Lys
225 230 235 240
Arg Val Asp Asp Met Leu Ala Ala Gly Leu Leu Glu Glu Leu Arg Asp
245 250 255
Phe His Arg Arg Tyr Asn Gln Lys Asn Val Ser Glu Asn Ser Gln Asp
260 265 270
Tyr Gln His Gly Ile Phe Gln Ser Ile Gly Phe Lys Glu Phe His Glu
275 280 285
Tyr Leu Ile Thr Glu Gly Lys Cys Thr Leu Glu Thr Ser Asn Gln Leu
290 295 300
Leu Lys Lys Gly Ile Glu Ala Leu Lys Gln Val Thr Lys Arg Tyr Ala
305 310 315 320
Arg Lys Gln Asn Arg Trp Val Lys Asn Arg Phe Leu Ser Arg Pro Gly
325 330 335
Pro Ile Val Pro Pro Val Tyr Gly Leu Glu Val Ser Asp Val Ser Lys
340 345 350
Trp Glu Glu Ser Val Leu Glu Pro Ala Leu Glu Ile Val Gln Ser Phe
355 360 365
Ile Gln Gly His Lys Pro Thr Ala Thr Pro Ile Lys Met Pro Tyr Asn
370 375 380
Glu Ala Glu Asn Lys Arg Ser Tyr His Leu Cys Asp Leu Cys Asp Arg
385 390 395 400
Ile Ile Ile Gly Asp Arg Glu Trp Ala Ala His Ile Lys Ser Lys Ser
405 410 415
His Leu Asn Gln Leu Lys Lys Arg Arg Arg Leu Asp Ser Asp Ala Val
420 425 430
Asn Thr Ile Glu Ser Gln Ser Val Ser Pro Asp His Asn Lys Glu Pro
435 440 445
Lys Glu Lys Gly Ser Pro Gly Gln Asn Asp Gln Glu Leu Lys Cys Ser

450 455 460
Val
465

<210> 152
<211> 2129
<212> DNA
<213> Homo sapiens

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aatccacgct ggcgttgcag ctaggccagc ggctcggcgg tgagatcgtc agcgctgact 180
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gaatctgccg gcaccacatg atcagctttg tggatcctct tgtgaccaat tacacagtgg 300
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<210> 153
<211> 467
<212> PRT
<213> Homo sapiens

<400> 153
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Arg Gly Leu Gln Arg Thr Leu Pro Leu Val Val Ile Leu Gly Ala Thr
20 25 30

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        35                  40                  45
Gly Glu Ile Val Ser Ala Asp Ser Met Gln Val Tyr Glu Gly Leu Asp
    50                  55                  60
Ile Ile Thr Asn Lys Val Ser Ala Gln Glu Gln Arg Ile Cys Arg His
65                  70                  75                  80
His Met Ile Ser Phe Val Asp Pro Leu Val Thr Asn Tyr Thr Val Val
                85                  90                  95
Asp Phe Arg Asn Arg Ala Thr Ala Leu Ile Glu Asp Ile Phe Ala Arg
            100                 105                 110
Asp Lys Ile Pro Ile Val Val Gly Gly Thr Asn Tyr Tyr Ile Glu Ser
        115                 120                 125
Leu Leu Trp Lys Val Leu Val Asn Thr Lys Pro Gln Glu Met Gly Thr
    130                 135                 140
Glu Lys Val Ile Asp Arg Lys Val Glu Leu Glu Lys Glu Asp Gly Leu
145                 150                 155                 160
Val Leu His Lys Arg Leu Ser Gln Val Asp Pro Glu Met Ala Ala Lys
                165                 170                 175
Leu His Pro His Asp Lys Arg Lys Val Ala Arg Ser Leu Gln Val Phe
            180                 185                 190
Glu Glu Thr Gly Ile Ser His Ser Glu Phe Leu His Arg Gln His Thr
        195                 200                 205
Glu Glu Gly Gly Gly Pro Leu Gly Gly Pro Leu Lys Phe Ser Asn Pro
    210                 215                 220
Cys Ile Leu Trp Leu His Ala Asp Gln Ala Val Leu Asp Glu Arg Leu
225                 230                 235                 240
Asp Lys Arg Val Asp Asp Met Leu Ala Ala Gly Leu Leu Glu Glu Leu
                245                 250                 255
Arg Asp Phe His Arg Arg Tyr Asn Gln Lys Asn Val Ser Glu Asn Ser
            260                 265                 270
Gln Asp Tyr Gln His Gly Ile Phe Gln Ser Ile Gly Phe Lys Glu Phe
        275                 280                 285
His Glu Tyr Leu Ile Thr Glu Gly Lys Cys Thr Leu Glu Thr Ser Asn
    290                 295                 300
Gln Leu Leu Lys Lys Gly Ile Glu Ala Leu Lys Gln Val Thr Lys Arg
305                 310                 315                 320
Tyr Ala Arg Lys Gln Asn Arg Trp Val Lys Asn Arg Phe Leu Ser Arg
                325                 330                 335
Pro Gly Pro Ile Val Pro Pro Val Tyr Gly Leu Glu Val Ser Asp Val
            340                 345                 350
Ser Lys Trp Glu Glu Ser Val Leu Glu Pro Ala Leu Glu Ile Val Gln
        355                 360                 365
Ser Phe Ile Gln Gly His Lys Pro Thr Ala Thr Pro Ile Lys Met Pro
    370                 375                 380
Tyr Asn Glu Ala Glu Asn Lys Arg Ser Tyr His Leu Cys Asp Leu Cys
385                 390                 395                 400
Asp Arg Ile Ile Ile Gly Asp Arg Glu Trp Ala Ala His Ile Lys Ser
                405                 410                 415
Lys Ser His Leu Asn Gln Leu Lys Lys Arg Arg Arg Leu Asp Ser Asp
            420                 425                 430
Ala Val Asn Thr Ile Glu Ser Gln Ser Val Ser Pro Asp His Asn Lys
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Glu Pro Lys Glu Lys Gly Ser Pro Gly Gln Asn Asp Gln Glu Leu Lys
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Cys Ser Val
465
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<210> 154
<211> 4495
<212> DNA
<213> Homo sapiens

<400> 154
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<210> 155
<211> 1066
<212> PRT
<213> Homo sapiens

<400> 155

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            20                  25                  30
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        35                  40                  45
Gly Ser Leu Phe Gly Tyr Ser Val Ala Leu His Arg Gln Thr Glu Arg
    50                  55                  60
Gln Gln Arg Tyr Leu Leu Leu Ala Gly Ala Pro Arg Glu Leu Ala Val
65                  70                  75                  80
Pro Asp Gly Tyr Thr Asn Arg Thr Gly Ala Val Tyr Leu Cys Pro Leu
                85                  90                  95
Thr Ala His Lys Asp Asp Cys Glu Arg Met Asn Ile Thr Val Lys Asn
            100                 105                 110
Asp Pro Gly His His Ile Ile Glu Asp Met Trp Leu Gly Val Thr Val
        115                 120                 125
Ala Ser Gln Gly Pro Ala Gly Arg Val Leu Val Cys Ala His Arg Tyr
    130                 135                 140
Thr Gln Val Leu Trp Ser Gly Ser Glu Asp Gln Arg Arg Met Val Gly
145                 150                 155                 160
Lys Cys Tyr Val Arg Gly Asn Asp Leu Glu Leu Asp Ser Ser Asp Asp
                165                 170                 175
Trp Gln Thr Tyr His Asn Glu Met Cys Asn Ser Asn Thr Asp Tyr Leu
            180                 185                 190
Glu Thr Gly Met Cys Gln Leu Gly Thr Ser Gly Gly Phe Thr Gln Asn
        195                 200                 205
Thr Val Tyr Phe Gly Ala Pro Gly Ala Tyr Asn Trp Lys Gly Asn Ser
    210                 215                 220
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Tyr Met Ile Gln Arg Lys Glu Trp Asp Leu Ser Glu Tyr Ser Tyr Lys
225                 230                 235                 240
Asp Pro Glu Asp Gln Gly Asn Leu Tyr Ile Gly Tyr Thr Met Gln Val
                245                 250                 255
Gly Ser Phe Ile Leu His Pro Lys Asn Ile Thr Ile Val Thr Gly Ala
            260                 265                 270
Pro Arg His Arg His Met Gly Ala Val Phe Leu Leu Ser Gln Glu Ala
        275                 280                 285
Gly Gly Asp Leu Arg Arg Arg Gln Val Leu Glu Gly Ser Gln Val Gly
    290                 295                 300
Ala Tyr Phe Gly Ser Ala Ile Ala Leu Ala Asp Leu Asn Asn Asp Gly
305                 310                 315                 320
Trp Gln Asp Leu Leu Val Gly Ala Pro Tyr Tyr Phe Glu Arg Lys Glu
                325                 330                 335
Glu Val Gly Gly Ala Ile Tyr Val Phe Met Asn Gln Ala Gly Thr Ser
            340                 345                 350
Phe Pro Ala His Pro Ser Leu Leu Leu His Gly Pro Ser Gly Ser Ala
        355                 360                 365
Phe Gly Leu Ser Val Ala Ser Ile Gly Asp Ile Asn Gln Asp Gly Phe
    370                 375                 380
Gln Asp Ile Ala Val Gly Ala Pro Phe Glu Gly Leu Gly Lys Val Tyr
385                 390                 395                 400
Ile Tyr His Ser Ser Ser Lys Gly Leu Leu Arg Gln Pro Gln Gln Val
                405                 410                 415
Ile His Gly Glu Lys Leu Gly Leu Pro Gly Leu Ala Thr Phe Gly Tyr
            420                 425                 430
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Val Lys Ala Arg Val Trp Asn Ser Thr Phe Ile Glu Asp Tyr Arg Asp
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Cys Gly Trp Cys Val Gln Glu Asp Phe Ile Ser Gly Gly Ser Arg Ser
65                  70                  75                  80
Glu Arg Cys Asp Ile Val Ser Asn Leu Ile Ser Lys Gly Cys Ser Val
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Asp Ser Ile Glu Tyr Pro Ser Val His Val Ile Ile Pro Thr Glu Asn
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Glu Ile Asn Thr Gln Val Thr Pro Gly Glu Val Ser Ile Gln Leu Arg
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Pro Gly Ala Glu Ala Asn Phe Met Leu Lys Val His Pro Leu Lys Lys
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Tyr Pro Val Asp Leu Tyr Tyr Leu Val Asp Val Ser Ala Ser Met His
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Arg Lys Glu Ala Lys Arg Leu Leu Leu Val Met Thr Asp Gln Thr Ser
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His Leu Ala Leu Asp Ser Lys Leu Ala Gly Ile Val Val Pro Asn Asp
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Gly Asn Cys His Leu Lys Asn Asn Val Tyr Val Lys Ser Thr Thr Met
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<211> 624
<212> PRT
<213> Homo sapiens

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Ser Ala Ile Ile Gly Gly Ser His Ser Lys Asn Tyr Val Leu Trp Glu
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Tyr Gly Gly Tyr Ala Ser Glu Gly Val Lys Gln Val Ala Glu Leu Gly
65 70 75 80
Ser Pro Val Lys Met Glu Glu Glu Ile Arg Gln Gln Ser Asp Glu Val
85 90 95
Leu Thr Val Ile Lys Ala Lys Ala Gln Trp Pro Ala Trp Gln Pro Leu
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Asn Val Arg Ala Ala Pro Ser Ala Glu Phe Ser Val Asp Arg Thr Arg
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His Leu Met Ser Phe Leu Thr Met Met Gly Pro Ser Pro Asp Trp Asn

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Gly Val Thr Tyr Glu Ser Pro Asn Lys Pro Thr Ile Pro Gln Glu Lys
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Ile Arg Pro Leu Thr Ser Leu Asp His Pro Gln Ser Pro Phe Tyr Asp
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Pro Glu Gly Gly Ser Ile Thr Gln Val Ala Arg Val Val Ile Glu Arg
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Asp Ile Val Ala Asp Leu Ala Pro Glu Glu Lys Asp Glu Asp Asp Thr
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Pro Glu Thr Cys Ile Tyr Ser Asn Trp Ser Pro Trp Ser Ala Cys Ser
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Ser Ser Thr Cys Asp Lys Gly Lys Arg Met Arg Gln Arg Met Leu Lys
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Ala Gln Leu Asp Leu Ser Val Pro Cys Pro Asp Thr Gln Asp Phe Gln
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Glu Glu Cys Ser Pro Ser Ser Cys Leu Met Thr Glu Trp Gly Glu Trp
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Asp Glu Cys Ser Ala Thr Cys Gly Met Gly Met Lys Lys Arg His Arg
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Met Ile Lys Met Asn Pro Ala Asp Gly Ser Met Cys Lys Ala Glu Thr
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Ser Gln Ala Glu Lys Cys Met Met Pro Glu Cys His Thr Ile Pro Cys
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Glu Cys Pro Ile Asp Cys Glu Leu Thr Glu Trp Ser Gln Trp Ser Glu
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Cys Asn Lys Ser Cys Gly Lys Gly His Val Ile Arg Thr Arg Met Ile
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Gln Met Glu Pro Gln Phe Gly Gly Ala Pro Cys Pro Glu Thr Val Gln
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Arg Lys Lys Cys Arg Ile Arg Lys Cys Leu Arg Asn Pro Ser Ile Gln
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Lys Leu Arg Trp Arg Glu Ala Arg Glu Ser Arg Arg Ser Glu Gln Leu
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Lys Glu Glu Ser Glu Gly Glu Gln Phe Pro Gly Cys Arg Met Arg Pro
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<212> DNA
<213> Homo sapiens

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<212> PRT
<213> Homo sapiens

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35 40 45
Leu Pro Lys Gln Tyr Leu Asp Val Ser Ser Gln Thr Asp Ile Ser Gly
50 55 60
Ser Phe Gly Ile Asn Ser Asn Asn Gln Leu Ala Glu Lys Val Arg Leu
65 70 75 80
Arg Leu Arg Tyr Glu Glu Ala Lys Arg Arg Ile Ala Asn Leu Lys Ile
85 90 95
Gln Leu Ala Lys Leu Asp Ser Glu Ala Trp Pro Gly Val Leu Asp Ser
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Glu Arg Asp Arg Leu Ile Leu Ile Asn Glu Lys Glu Glu Leu Leu Lys
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Glu Met Arg Phe Ile Ser Pro Arg Lys Trp Thr Gln Gly Glu Val Glu
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Gln Leu Glu Met Ala Arg Lys Arg Leu Glu Lys Asp Leu Gln Ala Ala
145 150 155 160
Arg Asp Thr Gln Ser Lys Ala Leu Thr Glu Arg Leu Lys Leu Asn Ser
165 170 175
Lys Arg Asn Gln Leu Val Arg Glu Leu Glu Glu Ala Thr Arg Gln Val
180 185 190
Ala Thr Leu His Ser Gln Leu Lys Ser Leu Ser Ser Ser Met Gln Ser
195 200 205
Leu Ser Ser Gly Ser Ser Pro Gly Ser Leu Thr Ser Ser Arg Gly Ser
210 215 220
Leu Val Ala Ser Ser Leu Asp Ser Ser Thr Ser Ala Ser Phe Thr Asp
225 230 235 240
Leu Tyr Tyr Asp Pro Phe Glu Gln Leu Asp Ser Glu Leu Gln Ser Lys
245 250 255
Val Glu Phe Leu Leu Leu Glu Gly Ala Thr Gly Phe Arg Pro Ser Gly
260 265 270
Cys Ile Thr Thr Ile His Glu Asp Glu Val Ala Lys Thr Gln Lys Ala
275 280 285
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290 295 300
Lys Ser Met Thr Ser Leu Ser Pro Arg Ser Ser Leu Ser Ser Pro Ser
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Glu Pro Gly Thr Glu Gly Lys Gln Leu Gly Gln Ala Val Asn Thr Ala
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Gln Gly Cys Gly Leu Lys Val Ala Cys Val Ser Ala Ala Val Ser Asp
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Glu Ser Val Ala Gly Asp Ser Gly Val Tyr Glu Ala Ser Val Gln Arg
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Lys Gln Phe Ala Ile Leu Ile Ile Gln Leu Ser Asn Leu Ser Ala Leu
    450                 455                 460
Leu Gln Gln Gln Asp Gln Lys Val Asn Ile Arg Val Ala Val Leu Pro
465                 470                 475                 480
Cys Ser Glu Ser Thr Thr Cys Leu Phe Arg Thr Arg Pro Leu Asp Ala
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Ser Asp Thr Leu Val Phe Asn Glu Val Phe Trp Val Ser Met Ser Tyr
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Ser Ser Thr Gln Thr Leu Glu Asp Ser Trp Arg Tyr Glu Glu Thr Ser
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Glu Gly Glu Glu Asp Val Phe Thr Glu Lys Ala Ser Pro Asp Met Asp
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Gly Tyr Pro Ala Leu Lys Val Asp Lys Glu Thr Asn Thr Glu Thr Pro
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Ala Pro Ser Pro Thr Val Val Arg Pro Lys Asp Arg Arg Val Gly Thr
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Pro Ser Gln Gly Pro Phe Leu Arg Gly Ser Thr Ile Ile Arg Ser Lys
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Thr Phe Ser Pro Gly Pro Gln Ser Gln Tyr Val Cys Arg Leu Asn Arg
705                 710                 715                 720
Ser Asp Ser Asp Ser Ser Thr Leu Ser Lys Lys Pro Pro Phe Val Arg
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Asn Ser Leu Glu Arg Arg Ser Val Arg Met Lys Arg Pro Ser Ser Val
            740                 745                 750
Lys Ser Leu Arg Ser Glu Arg Leu Ile Arg Thr Ser Leu Asp Leu Glu
        755                 760                 765
Leu Asp Leu Gln Ala Thr Arg Thr Trp His Ser Gln Leu Thr Gln Glu
    770                 775                 780
Ile Ser Val Leu Lys Glu Leu Lys Glu Gln Leu Glu Gln Ala Lys Ser
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His Gly Glu Lys Glu Leu Pro Gln Trp Leu Arg Glu Asp Glu Arg Phe
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            820                 825                 830
Lys Gly Glu Leu Gln Thr Asp Lys Met Met Arg Ala Ala Ala Lys Asp
        835                 840                 845
Val His Arg Leu Arg Gly Gln Ser Cys Lys Glu Pro Pro Glu Val Gln
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Met Arg Ala Pro His Leu His Leu Ser Ala Ala Ser Gly Ala Arg Ala
1 5 10 15
Leu Ala Lys Leu Leu Pro Leu Leu Met Ala Gln Leu Trp Ala Ala Glu
20 25 30
Ala Ala Leu Leu Pro Gln Asn Asp Thr Arg Leu Asp Pro Glu Ala Tyr
35 40 45
Gly Ala Pro Cys Ala Arg Gly Ser Gln Pro Trp Gln Val Ser Leu Phe
50 55 60
Asn Gly Leu Ser Phe His Cys Ala Gly Val Leu Val Asp Gln Ser Trp
65 70 75 80
Val Leu Thr Ala Ala His Cys Gly Asn Lys Pro Leu Trp Ala Arg Val
85 90 95
Gly Asp Asp His Leu Leu Leu Leu Gln Gly Glu Gln Leu Arg Arg Thr
100 105 110
Thr Arg Ser Val Val His Pro Lys Tyr His Gln Gly Ser Gly Pro Ile
115 120 125
Leu Pro Arg Arg Thr Asp Glu His Asp Leu Met Leu Leu Lys Leu Ala
130 135 140
Arg Pro Val Val Pro Gly Pro Arg Val Arg Ala Leu Gln Leu Pro Tyr
145 150 155 160
Arg Cys Ala Gln Pro Gly Asp Gln Cys Gln Val Ala Gly Trp Gly Thr
165 170 175
Thr Ala Ala Arg Arg Val Lys Tyr Asn Lys Gly Leu Thr Cys Ser Ser
180 185 190
Ile Thr Ile Leu Ser Pro Lys Glu Cys Glu Val Phe Tyr Pro Gly Val
195 200 205
Val Thr Asn Asn Met Ile Cys Ala Gly Leu Asp Arg Gly Gln Asp Pro
210 215 220
Cys Gln Ser Asp Ser Gly Gly Pro Leu Val Cys Asp Glu Thr Leu Gln
225 230 235 240
Gly Ile Leu Ser Trp Gly Val Tyr Pro Cys Gly Ser Ala Gln His Pro
245 250 255
Ala Val Tyr Thr Gln Ile Cys Lys Tyr Met Ser Trp Ile Asn Lys Val
260 265 270
Ile Arg Ser Asn
275

<210> 168
<211> 1506
<212> DNA
<213> Homo sapiens

<400> 168
aggcggacaa agcccgattg ttcctgggcc ctttccccat cgcgcctggg cctgctcccc 60
agcccggggc aggggcgggg gccagtgtgg tgacacacgc tgtagctgtc tccccggctg 120
gctggctcgc tctctcctgg ggacacagag gtcggcaggc agcacacaga gggacctacg 180
ggcagctgtt ccttcccccg actcaagaat ccccggaggc ccggaggcct gcagcaggag 240

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cggccatgaa gaagctgatg gtggtgctga gtctgattgc tgcagcctgg gcagaggagc 300
agaataagtt ggtgcatggc ggaccctgcg acaagacatc tcacccctac caagctgccc 360
tctacacctc gggccacttg ctctgtggtg ggtccttat ccatccactg tgggtcctca 420
cagctgccca ctgcaaaaaa ccgaatcttc aggtcttcct ggggaagcat aaccttcggc 480
aaagggagag ttcccaggag cagagttctg ttgtccgggc tgtgatccac cctgactatg 540
atgccgccag ccatgaccag gacatcatgc tgttgcgcct ggcacgccca gccaaactct 600
ctgaactcat ccagcccctt cccctggaga gggactgctc agccaacacc accagctgcc 660
acatcctggg ctggggcaag acagcagatg gtgatttccc tgacaccatc cagtgtgcat 720
acatccacct ggtgtcccgt gaggagtgtg agcatgccta ccctggccag atcacccaga 780
acatgttgtg tgctggggat gagaagtacg ggaaggattc ctgccagggt gattctgggg 840
gtccgctggt atgtggagac cacctccgag gccttgtgtc atggggtaac atcccctgtg 900
gatcaaagga gaagccagga gtctacacca acgtctgcag atacacgaac tggatccaaa 960
aaaccattca ggccaagtga ccctgacatg tgacatctac ctcccgacct accaccccac 1020
tggctggttc cagaacgtct ctcacctaga ccttgcctcc cctcctctcc tgcccagctc 1080
tgaccctgat gcttaataaa cgcagcgacg tgagggtcct gattctccct ggttttaccc 1140
cagctccatc cttgcatcac tggggaggac gtgatgagtg aggacttggg tcctcggtct 1200
tacccccacc actaagagaa tacaggaaaa tcccttctag gcatctcctc tccccaaccc 1260
ttccacacgt ttgatttctt cctgcagagg cccagccacg tgtctggaat cccagctccg 1320
ctgcttactg tcggtgtccc cttgggatgt acctttcttc actgcagatt tctcacctgt 1380
aagatgaaga taaggatgat acagtctcca tcaggcagtg gctgttggaa agatttaaga 1440
tttcacacct atgacataca tgggatagca cctgggccgc catgcactca ataaagaatg 1500
tatttt                                                            1506
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<210> 169
<211> 244
<212> PRT
<213> Homo sapiens

<400> 169

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Met Lys Lys Leu Met Val Val Leu Ser Leu Ile Ala Ala Ala Trp Ala
 1               5                  10                  15
Glu Glu Gln Asn Lys Leu Val His Gly Gly Pro Cys Asp Lys Thr Ser
            20                  25                  30
His Pro Tyr Gln Ala Ala Leu Tyr Thr Ser Gly His Leu Leu Cys Gly
        35                  40                  45
Gly Val Leu Ile His Pro Leu Trp Val Leu Thr Ala Ala His Cys Lys
    50                  55                  60
Lys Pro Asn Leu Gln Val Phe Leu Gly Lys His Asn Leu Arg Gln Arg
65                  70                  75                  80
Glu Ser Ser Gln Glu Gln Ser Ser Val Val Arg Ala Val Ile His Pro
                85                  90                  95
Asp Tyr Asp Ala Ala Ser His Asp Gln Asp Ile Met Leu Leu Arg Leu
            100                 105                 110
Ala Arg Pro Ala Lys Leu Ser Glu Leu Ile Gln Pro Leu Pro Leu Glu
        115                 120                 125
Arg Asp Cys Ser Ala Asn Thr Thr Ser Cys His Ile Leu Gly Trp Gly
    130                 135                 140
Lys Thr Ala Asp Gly Asp Phe Pro Asp Thr Ile Gln Cys Ala Tyr Ile
145                 150                 155                 160
His Leu Val Ser Arg Glu Glu Cys Glu His Ala Tyr Pro Gly Gln Ile
                165                 170                 175
Thr Gln Asn Met Leu Cys Ala Gly Asp Glu Lys Tyr Gly Lys Asp Ser
            180                 185                 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Gly Asp His Leu Arg
        195                 200                 205
Gly Leu Val Ser Trp Gly Asn Ile Pro Cys Gly Ser Lys Glu Lys Pro
    210                 215                 220
Gly Val Tyr Thr Asn Val Cys Arg Tyr Thr Asn Trp Ile Gln Lys Thr
```

225 230 235 240
Ile Gln Ala Lys

<210> 170
<211> 1641
<212> DNA
<213> Homo sapiens

<400> 170
agcgagtgcg cgctcctcct cgcccgccgc taggtccatc ccggcccagc caccatgtcc 60
atccacttca gctccccggt attcacctcg cgctcagccg ccttctcggg ccgcggcgcc 120
caggtgcgcc tgagctccgc tcgcccggc ggccttggca gcagcagcct ctacggcctc 180
ggcgcctcgc ggccgcgcgt ggccgtgcgc tctgcctatg gggcccggt gggcgccggc 240
atccgcgagg tcaccattaa ccagagcctg ctggccccgc tgcggctgga cgccgacccc 300
tccctccagc gggtgcgcca ggaggagagc gagcagatca agaccctcaa caacaagttt 360
gcctccttca tcgacaaggt gcggtttctg gagcagcaga acaagctgct ggagaccaag 420
tggacgctgc tgcaggagca gaagtcggcc aagagcagcc gcctcccaga catctttgag 480
gcccagattg ctggccttcg gggtcagctt gaggcactgc aggtggatgg gggccgcctg 540
gaggcggagc tgcggagcat gcaggatgtg gtggaggact tcaagaataa gtacgaagat 600
gaaattaacc gccgcacagc tgctgagaat gagtttgtgg tgctgaagaa ggatgtggat 660
gctgcctaca cgagcaaggt ggagctggag gccaaggtgg atgccctgaa tgatgagatc 720
aacttcctca ggaccctcaa tgagacggag ttgacagagc tgcagtccca gatctccgac 780
acatctgtgg tgctgtccat ggacaacagt cgctccctgg acctggacgg catcatcgct 840
gaggtcaagg cacagtatga ggagatggcc aaatgcagcc gggctgaggc tgaagcctgg 900
taccagacca agtttgagac cctccaggcc caggctggga agcatgggga cgacctccgg 960
aatacccgga atgagatttc agagatgaac cgggccatcc agaggctgca ggctgagatc 1020
gacaacatca agaaccagcg tgccaagttg gaggccgcca ttgccgaggc tgaggagcgt 1080
ggggagctgg cgctcaagga tgctcgtgcc aagcaggagg agctggaagc cgccctgcag 1140
cgggccaagc aggatatggc acggcagctg cgtgagtacc aggaactcat gagcgtgaag 1200
ctggccctgg acatcgagat cgccacctac cgcaagctgc tggagggcga ggagagccgg 1260
ttggctggag atggagtggg agccgtgaat atctctgtga tgaattccac tggtggcagt 1320
agcagtggcg gtggcattgg gctgaccctc gggggaacca tgggcagcaa tgccctgagc 1380
ttctccagca gtgcgggtcc tgggctcctg aaggcttatt ccatccggac cgcatccgcc 1440
agtcgcagga gtgcccgcga ctgagccgcc tcccaccact ccactcctcc agccaccacc 1500
cacaatcaca agaagattcc cacccctgcc tcccatgcct ggtcccaaga cagtgagaca 1560
gtctggaaag tgatgtcaga atagcttcca ataaagcagc ctcattctga ggcctgagtg 1620
atccaaaaaa aaaaaaaaaa a 1641

<210> 171
<211> 469
<212> PRT
<213> Homo sapiens

<400> 171
Met Ser Ile His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala
1 5 10 15
Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly
20 25 30
Gly Leu Gly Ser Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg
35 40 45
Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg
50 55 60
Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala
65 70 75 80
Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys
85 90 95

```
Ala Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu
            100                 105                 110
Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu
        115                 120                 125
Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln
    130                 135                 140
Ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly
145                 150                 155                 160
Arg Leu Glu Gln Gly Leu Arg Thr Met Gln Asp Val Val Glu Asp Phe
                165                 170                 175
Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn
            180                 185                 190
Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys
        195                 200                 205
Val Glu Leu Glu Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe
    210                 215                 220
Leu Arg Thr Leu Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile
225                 230                 235                 240
Ser Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp
                245                 250                 255
Leu Asp Gly Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala
            260                 265                 270
Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu
        275                 280                 285
Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr
    290                 295                 300
Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala
305                 310                 315                 320
Glu Ile Asp Asn Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile
                325                 330                 335
Ala Glu Ala Glu Glu Cys Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala
            340                 345                 350
Lys Gln Glu Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met
        355                 360                 365
Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala
    370                 375                 380
Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu
385                 390                 395                 400
Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met
                405                 410                 415
Asn Ser Thr Gly Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu
            420                 425                 430
Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly
        435                 440                 445
Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg
    450                 455                 460
Arg Ser Ala Arg Asp
465
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<210> 172
<211> 1640
<212> DNA
<213> Homo sapiens

<400> 172
gcgagtgcgc gctcctcctc gcccgccgct aggtccatcc cggcccagcc accatgtcca 60
tccacttcag ctccccggta ttcacctcgc gctcagccgc cttctcgggc cgcggcgccc 120

aggtgcgcct gagctccgct cgccccggcg gccttggcag cagcagcctc tacggcctcg 180
gcgcctcgcg gccgcgcgtg gccgtgcgct ctgcctatgg gggcccggtg ggcgccggca 240
tccgcgaggt caccattaac cagagcctgc tggccccgct gcggctggac gccgacccct 300
ccctccagcg ggtgcgccag gaggagagcg agcagatcaa gaccctcaac aacaagtttg 360
cctccttcat cgacaaggtg cggtttctgg agcagcagaa caagctgctg gagaccaagt 420
ggacgctgct gcaggagcag aagtcggcca agagcagccg cctcccagac atctttgagg 480
cccagattgc tggccttcgg ggtcagcttg aggcactgca ggtggatggg ggccgcctgg 540
aggcggagct gcggagcatg caggatgtgg tggaggactt caagaataag tacgaagatg 600
aaattaaccg ccgcacagct gctgagaatg agtttgtggt gctgaagaag gatgtggatg 660
ctgcctacat gagcaaggtg gagctggagg ccaaggtgga tgccctgaat gatgagatca 720
acttcctcag gaccctcaat gagacggagt tgacagagct gcagtcccag atctccgaca 780
catctgtggt gctgtccatg gacaacagtc gctccctgga cctggacggc atcatcgctg 840
aggtcaaggc acagtatgag gagatggcca aatgcagccg ggctgaggct gaagcctggt 900
accagaccaa gtttgagacc ctccaggccc aggctgggaa gcatggggac gacctccgga 960
atacccggaa tgagatttca gagatgaacc gggccatcca gaggctgcag gctgagatcg 1020
acaacatcaa gaaccagcgt gccaagttgg aggccgccat tgccgaggct gaggagcgtg 1080
gggagctggc gctcaaggat gctcgtgcca agcaggagga gctggaagcc gccctgcagc 1140
gggccaagca ggatatggca cggcagctgc gtgagtacca ggaactcatg agcgtgaagc 1200
tggccctgga catcgagatc gccacctacc gcaagctgct ggagggcgag gagagccggt 1260
tggctggaga tggagtggga gccgtgaata tctctgtgat gaattccact ggtggcagta 1320
gcagtggcgg tggcattggg ctgaccctcg ggggaaccat gggcagcaat gccctgagct 1380
tctccagcag tgcgggtcct gggctcctga aggcttattc catccggacc gcatccgcca 1440
gtcgcaggag tgcccgcgac tgagccgcct cccaccactc cactcctcca gccaccaccc 1500
acaatcacaa gaagattccc acccctgcct cccatgcctg gtcccaagac agtgagacag 1560
tctggaaagt gatgtcagaa tagcttccaa taaagcagcc tcattctgag gcctgagtga 1620
tccaaaaaaa aaaaaaaaaa 1640

<210> 173
<211> 469
<212> PRT
<213> Homo sapiens

<400> 173
Met Ser Ile His Phe Ser Ser Pro Val Phe Thr Ser Arg Ser Ala Ala
1 5 10 15
Phe Ser Gly Arg Gly Ala Gln Val Arg Leu Ser Ser Ala Arg Pro Gly
20 25 30
Gly Leu Gly Ser Ser Ser Leu Tyr Gly Leu Gly Ala Ser Arg Pro Arg
35 40 45
Val Ala Val Arg Ser Ala Tyr Gly Gly Pro Val Gly Ala Gly Ile Arg
50 55 60
Glu Val Thr Ile Asn Gln Ser Leu Leu Ala Pro Leu Arg Leu Asp Ala
65 70 75 80
Asp Pro Ser Leu Gln Arg Val Arg Gln Glu Glu Ser Glu Gln Ile Lys
85 90 95
Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu
100 105 110
Glu Gln Gln Asn Lys Leu Leu Glu Thr Lys Trp Thr Leu Leu Gln Glu
115 120 125
Gln Lys Ser Ala Lys Ser Ser Arg Leu Pro Asp Ile Phe Glu Ala Gln
130 135 140
Ile Ala Gly Leu Arg Gly Gln Leu Glu Ala Leu Gln Val Asp Gly Gly
145 150 155 160
Arg Leu Glu Ala Glu Leu Arg Ser Met Gln Asp Val Val Glu Asp Phe
165 170 175
Lys Asn Lys Tyr Glu Asp Glu Ile Asn Arg Arg Thr Ala Ala Glu Asn
180 185 190
Glu Phe Val Val Leu Lys Lys Asp Val Asp Ala Ala Tyr Met Ser Lys

```
        195                 200                 205
Val Glu Leu Glu Ala Lys Val Asp Ala Leu Asn Asp Glu Ile Asn Phe
    210                 215                 220
Leu Arg Thr Leu Asn Glu Thr Glu Leu Thr Glu Leu Gln Ser Gln Ile
225                 230                 235                 240
Ser Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp
                245                 250                 255
Leu Asp Gly Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Glu Met Ala
            260                 265                 270
Lys Cys Ser Arg Ala Glu Ala Glu Ala Trp Tyr Gln Thr Lys Phe Glu
        275                 280                 285
Thr Leu Gln Ala Gln Ala Gly Lys His Gly Asp Asp Leu Arg Asn Thr
    290                 295                 300
Arg Asn Glu Ile Ser Glu Met Asn Arg Ala Ile Gln Arg Leu Gln Ala
305                 310                 315                 320
Glu Ile Asp Asn Ile Lys Asn Gln Arg Ala Lys Leu Glu Ala Ala Ile
                325                 330                 335
Ala Glu Ala Glu Glu Arg Gly Glu Leu Ala Leu Lys Asp Ala Arg Ala
            340                 345                 350
Lys Gln Glu Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met
        355                 360                 365
Ala Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Ser Val Lys Leu Ala
    370                 375                 380
Leu Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu
385                 390                 395                 400
Ser Arg Leu Ala Gly Asp Gly Val Gly Ala Val Asn Ile Ser Val Met
                405                 410                 415
Asn Ser Thr Gly Gly Ser Ser Ser Gly Gly Gly Ile Gly Leu Thr Leu
            420                 425                 430
Gly Gly Thr Met Gly Ser Asn Ala Leu Ser Phe Ser Ser Ser Ala Gly
        435                 440                 445
Pro Gly Leu Leu Lys Ala Tyr Ser Ile Arg Thr Ala Ser Ala Ser Arg
    450                 455                 460
Arg Ser Ala Arg Asp
465
```

<210> 174
<211> 2186
<212> DNA
<213> Homo sapiens

<400> 174

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acacggacca aggagtctaa cacgtgcgcg agtcgggggc tcgcacgaaa gccgccgtgg 60
cgcaatgaag gtgaaggccg gcgcgctcgc cggccgaggt gggatcccga ggcctctcca 120
gtccgccgag ggcgcaccac cggcccgtct cgcccgccgc gccggggagg tggagcacga 180
gcgcacgtgt taggacccga aagatggtga actatgcctg ggcagggcga agccagagga 240
aactctggtg gaggtccgta gcggtcctga cgtgcaaatc ggtcgtccga cctgggtata 300
ggggcgggct ccaggcgagg cggtcgacgc tcctgaaaac ttgcgcgcgc gctcgcgcca 360
ctgcgcccgg agcgatgaag atggtcgcgc cctggacgcg gttctactcc aacagctgct 420
gcttgtgctg ccatgtccgc accggcacca tcctgctcgg cgtctggtat ctgatcatca 480
atgctgtggt actgttgatt ttattgagtg ccctggctga tccggatcag tataactttt 540
caagttctga actgggaggt gactttgagt tcatggatga tgccaacatg tgcattgcca 600
ttgcgatttc tcttctcatg atcctgatat gtgctatggc tacttacgga gcgtacaagc 660
aacgcgcagc ctggatcatc ccattcttct gttaccagat ctttgacttt gccctgaaca 720
tgttggttgc aatcactgtg cttatttatc caaactccat tcaggaatac atacggcaac 780
tgcctcctaa ttttccctac agagatgatg tcatgtcagt gaatcctacc tgtttggtcc 840
ttattattct tctgtttatt agcattatct tgacttttaa gggttacttg attagctgtg 900
```

```
tttggaactg ctaccgatac atcaatggta ggaactcctc tgatgtcctg gtttatgtta 960
ccagcaatga cactacggtg ctgctacccc cgtatgatga tgccactgtg aatggtgctg 1020
ccaaggagcc accgccacct tacgtgtctg cctaagcctt caagtgggcg gagctgaggg 1080
cagcagcttg actttgcaga catctgagca atagttctgt tatttcactt ttgccatgag 1140
cctctctgag cttgtttgtt gctgaaatgc tactttttaa aatttagatg ttagattgaa 1200
aactgtagtt ttcaacatat gctttgctag aacactgtga tagattaact gtagaattct 1260
tcctgtacga ttggggatat aatgggcttc actaaccttc cctaggcatt gaaacttccc 1320
ccaaatctga tggacctaga agtctgcttt tgtacctgct gggccccaaa gttgggcatt 1380
tttctctctg ttccctctct tttgaaaatg taaaataaaa ccaaaaatag acaacttttt 1440
cttcagccat tccagcatag agaacaaaac cttatggaaa caggaatgtc aattgtgtaa 1500
tcattgttct aattaggtaa atagaagtcc ttatgtatgt gttacaagaa tttcccccac 1560
aacatccttt atgactgaag ttcaatgaca gtttgtgttt gggtggtaaa ggattttctc 1620
catggcctga attaagacca ttagaaagca ccaggccgtg ggagcagtga ccatctgctg 1680
actgttcttg tggatcttgt gtccagggac atggggtgac atgcctcgta tgtgttagag 1740
ggtggaatgg atgtgtttgg cgctgcatgg gatctggtgc ccctcttctc ctggattcac 1800
atccccaccc agggcccgct tttactaagt gttctgccct agattggttc aaggaggtca 1860
tccaactgac tttatcaagt ggaattggga tatatttgat atacttctgc ctaacaacat 1920
ggaaaagggt tttcttttcc ctgcaagcta catcctactg ctttgaactt ccaagtatgt 1980
ctagtcacct tttaaaatgt aaacattttc agaaaaatga ggattgcctt ccttgtatgc 2040
gctttttacc ttgactacct gaattgcaag ggatttttat atattcatat gttacaaagt 2100
cagcaactct cctgttggtt cattattgaa tgtgctgtaa attaagttgt ttgcaattaa 2160
aacaaggttt gcccacaaaa aaaaaa                                      2186

<210> 175
<211> 283
<212> PRT
<213> Homo sapiens

<400> 175
Met Val Asn Tyr Ala Trp Ala Gly Arg Ser Gln Arg Lys Leu Trp Trp
 1               5                  10                  15
Arg Ser Val Ala Val Leu Thr Cys Lys Ser Val Val Arg Pro Gly Tyr
            20                  25                  30
Arg Gly Gly Leu Gln Ala Arg Arg Ser Thr Leu Leu Lys Thr Cys Ala
        35                  40                  45
Arg Ala Arg Ala Thr Ala Pro Gly Ala Met Lys Met Val Ala Pro Trp
    50                  55                  60
Thr Arg Phe Tyr Ser Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr
65                  70                  75                  80
Gly Thr Ile Leu Leu Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val
                85                  90                  95
Leu Leu Ile Leu Leu Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe
            100                 105                 110
Ser Ser Ser Glu Leu Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn
        115                 120                 125
Met Cys Ile Ala Ile Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala
    130                 135                 140
Met Ala Thr Tyr Gly Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro
145                 150                 155                 160
Phe Phe Cys Tyr Gln Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala
                165                 170                 175
Ile Thr Val Leu Ile Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln
            180                 185                 190
Leu Pro Pro Asn Phe Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro
        195                 200                 205
Thr Cys Leu Val Leu Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr
    210                 215                 220
Phe Lys Gly Tyr Leu Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile
```

```
225                 230                 235                 240
Asn Gly Arg Asn Ser Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp
                245                 250                 255
Thr Thr Val Leu Leu Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala
            260                 265                 270
Ala Lys Glu Pro Pro Pro Pro Tyr Val Ser Ala
        275                 280
```

<210> 176
<211> 597
<212> DNA
<213> Homo sapiens

<400> 176

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atgcccctag gtctcctgtg gctgggccta gccctgttgg gggctctgca tgcccaggcc 60
caggactcca cctcagacct gatcccagcc ccacctctga gcaaggtccc tctgcagcag 120
aacttccagg acaaccaatt ccaggggaag tggtatgtgg taggcctggc agggaatgca 180
attctcagag aagacaaaga cccgcaaaag atgtatgcca ccatctatga gctgaaagaa 240
gacaagagct acaatgtcac ctccgtcctg tttaggaaaa agaagtgtga ctactggatc 300
aggacttttg ttccaggttg ccagcccggc gagttcacgc tgggcaacat taagagttac 360
cctggattaa cgagttacct cgtccgagtg gtgagcacca actacaacca gcatgctatg 420
gtgttcttca agaaagtttc tcaaaacagg gagtacttca agatcaccct ctacgggaga 480
accaaggagc tgacttcgga actaaaggag aacttcatcc gcttctccaa atatctgggc 540
ctccctgaaa accacatcgt cttccctgtc ccaatcgacc agtgtatcga cggctga    597
```

<210> 177
<211> 198
<212> PRT
<213> Homo sapiens

<400> 177

```
Met Pro Leu Gly Leu Leu Trp Leu Gly Leu Ala Leu Leu Gly Ala Leu
1               5                   10                  15
His Ala Gln Ala Gln Asp Ser Thr Ser Asp Leu Ile Pro Ala Pro Pro
            20                  25                  30
Leu Ser Lys Val Pro Leu Gln Gln Asn Phe Gln Asp Asn Gln Phe Gln
        35                  40                  45
Gly Lys Trp Tyr Val Val Gly Leu Ala Gly Asn Ala Ile Leu Arg Glu
    50                  55                  60
Asp Lys Asp Pro Gln Lys Met Tyr Ala Thr Ile Tyr Glu Leu Lys Glu
65                  70                  75                  80
Asp Lys Ser Tyr Asn Val Thr Ser Val Leu Phe Arg Lys Lys Lys Cys
                85                  90                  95
Asp Tyr Trp Ile Arg Thr Phe Val Pro Gly Cys Gln Pro Gly Glu Phe
            100                 105                 110
Thr Leu Gly Asn Ile Lys Ser Tyr Pro Gly Leu Thr Ser Tyr Leu Val
        115                 120                 125
Arg Val Val Ser Thr Asn Tyr Asn Gln His Ala Met Val Phe Phe Lys
    130                 135                 140
Lys Val Ser Gln Asn Arg Glu Tyr Phe Lys Ile Thr Leu Tyr Gly Arg
145                 150                 155                 160
Thr Lys Glu Leu Thr Ser Glu Leu Lys Glu Asn Phe Ile Arg Phe Ser
                165                 170                 175
Lys Tyr Leu Gly Leu Pro Glu Asn His Ile Val Phe Pro Val Pro Ile
            180                 185                 190
Asp Gln Cys Ile Asp Gly
        195
```

<210> 178
<211> 1518
<212> DNA
<213> Homo sapiens

<400> 178
```
gcctgagacc ctcctgcagc cttctcaagg gacagcccca ctctgcctct tgctcctcca 60
gggcagcacc atgcagcccc tgtggctctg ctgggcactc tgggtgttgc cctggccag 120
ccccggggcc gccctgaccg gggagcagct cctgggcagc ctgctgcggc agctgcagct 180
caaagaggtg cccaccctgg acagggccga catggaggag ctggtcatcc ccacccacgt 240
gagggcccag tacgtggccc tgctgcagcg cagccacggg gaccgctccc gcggaaagag 300
gttcagccag agcttccgag aggtggccgg caggttcctg gcgttggagg ccagcacaca 360
cctgctggtg ttcggcatgg agcagcggct gccgcccaac agcgagctgg tgcaggccgt 420
gctgcggctc ttccaggagc cggtccccaa ggccgcgctg cacaggcacg ggcggctgtc 480
cccgcgcagc gcccgggccc gggtgaccgt cgagtggctg cgcgtccgcg acgacggctc 540
caaccgcacc tccctcatcg actccaggct ggtgtccgtc cacgagagcg gctggaaggc 600
cttcgacgtg accgaggccg tgaacttctg gcagcagctg agccggcccc ggcagccgct 660
gctgctacag gtgtcggtgc agagggagca tctgggcccg ctggcgtccg gcgcccacaa 720
gctggtccgc tttgcctcgc agggggcgcc agccgggctt ggggagcccc agctggagct 780
gcacaccctg gaccttgggg actatggagc tcagggcgac tgtgaccctg aagcaccaat 840
gaccgagggc acccgctgct gccgccagga gatgtacatt gacctgcagg ggatgaagtg 900
ggccgagaac tgggtgctgg agcccccggg cttcctggct tatgagtgtg tgggcacctg 960
ccggcagccc ccggaggccc tggccttcaa gtggccgttt ctggggcctc gacagtgcat 1020
cgcctcggag actgactcgc tgcccatgat cgtcagcatc aaggagggag gcaggaccag 1080
gccccaggtg gtcagcctgc ccaacatgag ggtgcagaag tgcagctgtg cctcggatgg 1140
tgcgctcgtg ccaaggaggc tccagccata ggcgcctagt gtagccatcg agggacttga 1200
cttgtgtgtg tttctgaagt gttcgagggt accaggagag ctggcgatga ctgaactgct 1260
gatggacaaa tgctctgtgc tctctagtga gccctgaatt tgcttcctct gacaagttac 1320
ctcacctaat tttgcttctc caggaatgag aatctttggc cactggagag cccttgctca 1380
gttttctcta ttcttattat tcactgcact atattctaag cacttacatg tggagatact 1440
gtaacctgag ggcagaaagc ccaatgtgtc attgtttact tgtcctgtca ctggatctgg 1500
gctaaagtcc tccaccac                                                1518
```

<210> 179
<211> 366
<212> PRT
<213> Homo sapiens

<400> 179
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Met Gln Pro Leu Trp Leu Cys Trp Ala Leu Trp Val Leu Pro Leu Ala
1               5                   10                  15
Ser Pro Gly Ala Ala Leu Thr Gly Glu Gln Leu Leu Gly Ser Leu Leu
            20                  25                  30
Arg Gln Leu Gln Leu Lys Glu Val Pro Thr Leu Asp Arg Ala Asp Met
        35                  40                  45
Glu Glu Leu Val Ile Pro Thr His Val Arg Ala Gln Tyr Val Ala Leu
    50                  55                  60
Leu Gln Arg Ser His Gly Asp Arg Ser Arg Gly Lys Arg Phe Ser Gln
65                  70                  75                  80
Ser Phe Arg Glu Val Ala Gly Arg Phe Leu Ala Leu Glu Ala Ser Thr
                85                  90                  95
His Leu Leu Val Phe Gly Met Glu Gln Arg Leu Pro Pro Asn Ser Glu
            100                 105                 110
Leu Val Gln Ala Val Leu Arg Leu Phe Gln Glu Pro Val Pro Lys Ala
        115                 120                 125
Ala Leu His Arg His Gly Arg Leu Ser Pro Arg Ser Ala Arg Ala Arg
```

```
    130                 135                 140
Val Thr Val Glu Trp Leu Arg Val Arg Asp Asp Gly Ser Asn Arg Thr
145                 150                 155                 160
Ser Leu Ile Asp Ser Arg Leu Val Ser Val His Glu Ser Gly Trp Lys
                165                 170                 175
Ala Phe Asp Val Thr Glu Ala Val Asn Phe Trp Gln Gln Leu Ser Arg
            180                 185                 190
Pro Arg Gln Pro Leu Leu Leu Gln Val Ser Val Gln Arg Glu His Leu
        195                 200                 205
Gly Pro Leu Ala Ser Gly Ala His Lys Leu Val Arg Phe Ala Ser Gln
    210                 215                 220
Gly Ala Pro Ala Gly Leu Gly Glu Pro Gln Leu Glu Leu His Thr Leu
225                 230                 235                 240
Asp Leu Gly Asp Tyr Gly Ala Gln Gly Asp Cys Asp Pro Glu Ala Pro
                245                 250                 255
Met Thr Glu Gly Thr Arg Cys Cys Arg Gln Glu Met Tyr Ile Asp Leu
            260                 265                 270
Gln Gly Met Lys Trp Ala Glu Asn Trp Val Leu Glu Pro Pro Gly Phe
        275                 280                 285
Leu Ala Tyr Glu Cys Val Gly Thr Cys Arg Gln Pro Pro Glu Ala Leu
    290                 295                 300
Ala Phe Lys Trp Pro Phe Leu Gly Pro Arg Gln Cys Ile Ala Ser Glu
305                 310                 315                 320
Thr Asp Ser Leu Pro Met Ile Val Ser Ile Lys Glu Gly Gly Arg Thr
                325                 330                 335
Arg Pro Gln Val Val Ser Leu Pro Asn Met Arg Val Gln Lys Cys Ser
            340                 345                 350
Cys Ala Ser Asp Gly Ala Leu Val Pro Arg Arg Leu Gln Pro
        355                 360                 365
```

<210> 180
<211> 444
<212> DNA
<213> Homo sapiens

<400> 180

```
aattctagaa gtccaaatca ctcattgttt gtgaaagctg agctcacagc aaaacaagcc 60
accatgaagc tgtcggtgtg tctcctgctg gtcacgctgg ccctctgctg ctaccaggcc 120
aatgccgagt tctgcccagc tcttgtttct gagctgttag acttcttctt cattagtgaa 180
cctctgttca agttaagtct tgccaaattt gatgcccctc cggaagctgt tgcagccaag 240
ttaggagtga agagatgcac ggatcagatg tcccttcaga aacgaagcct cattgcggaa 300
gtcctggtga aaatattgaa gaaatgtagt gtgtgacatg taaaaacttt catcctggtt 360
tccactgtct ttcaatgaca ccctgatctt cactgcagaa tgtaaaggtt tcaacgtctt 420
gctttaataa atcacttgct ctac                                        444
```

<210> 181
<211> 90
<212> PRT
<213> Homo sapiens

<400> 181

```
Met Lys Leu Ser Val Cys Leu Leu Leu Val Thr Leu Ala Leu Cys Cys
 1               5                  10                  15
Tyr Gln Ala Asn Ala Glu Phe Cys Pro Ala Leu Val Ser Glu Leu Leu
            20                  25                  30
Asp Phe Phe Phe Ile Ser Glu Pro Leu Phe Lys Leu Ser Leu Ala Lys
        35                  40                  45
```

```
Phe Asp Ala Pro Pro Glu Ala Val Ala Ala Lys Leu Gly Val Lys Arg
    50                  55                  60
Cys Thr Asp Gln Met Ser Leu Gln Lys Arg Ser Leu Ile Ala Glu Val
65                  70                  75                  80
Leu Val Lys Ile Leu Lys Lys Cys Ser Val
                85                  90
```

<210> 182
<211> 754
<212> DNA
<213> Homo sapiens

<400> 182

```
ggagtatgag atgaaacgaa tggcagagaa tgagctgagc cggtcagtaa atgagtttct 60
gtccaagctg caagatgacc tcaaggaggc aatgaatact atgatgtgta gccgatgcca 120
aggaaagcat aggaggtttg aaatggaccg ggaacctaag agtgccagat actgtgctga 180
gtgtaatagg ctgcatcctg ctgaggaagg agacttttgg gcagagtcaa gcatgttggg 240
cctcaagatc acctactttg cactgatgga tggaaaggtg tatgacatca cagagtgggc 300
tggatgccag cgtgtaggta tctccccaga tacccacaga gtcccctatc acatctcatt 360
tggttctcgg attccaggca ccagagggcg gcagagagcc accccagatg cccctcctgc 420
tgatcttcag gatttcttga gtcggatctt tcaagtaccc ccagggcaga tgccaatggg 480
aacttctttg cagctcctca gcctgcccct ggagccgctg cagcctctaa gcccaacagc 540
acagtaccca agggagaagc caaacctaag cggcggaaga aagtgaggag gcccttccaa 600
cgttgatgcc ccttctcttt cctcaaatca atgtcaggga gtcaaaaggg ctgtagcaca 660
ggatggagtt tgatttatcc ctcctccccc aacacctagg aactgaatct tttcttttt 720
attttttgag atggagtctt gctctgttgc ccag                             754
```

<210> 183
<211> 191
<212> PRT
<213> Homo sapiens

<400> 183

```
Met Lys Arg Met Ala Glu Asn Glu Leu Ser Arg Ser Val Asn Glu Phe
 1               5                  10                  15
Leu Ser Lys Leu Gln Asp Asp Leu Lys Glu Ala Met Asn Thr Met Met
            20                  25                  30
Cys Ser Arg Cys Gln Gly Lys His Arg Arg Phe Glu Met Asp Arg Glu
        35                  40                  45
Pro Lys Ser Ala Arg Tyr Cys Ala Glu Cys Asn Arg Leu His Pro Ala
    50                  55                  60
Glu Glu Gly Asp Phe Trp Ala Glu Ser Ser Met Leu Gly Leu Lys Ile
65                  70                  75                  80
Thr Tyr Phe Ala Leu Met Asp Gly Lys Val Tyr Asp Ile Thr Glu Trp
                85                  90                  95
Ala Gly Cys Gln Arg Val Gly Ile Ser Pro Asp Thr His Arg Val Pro
            100                 105                 110
Tyr His Ile Ser Phe Gly Ser Arg Ile Pro Gly Thr Arg Gly Arg Gln
        115                 120                 125
Arg Ala Thr Pro Asp Ala Pro Pro Ala Asp Leu Gln Asp Phe Leu Ser
    130                 135                 140
Arg Ile Phe Gln Val Pro Pro Gly Gln Met Pro Met Gly Thr Ser Leu
145                 150                 155                 160
Gln Leu Leu Ser Leu Pro Leu Glu Pro Leu Gln Pro Leu Ser Pro Thr
                165                 170                 175
Ala Gln Tyr Pro Arg Glu Lys Pro Asn Leu Ser Gly Gly Arg Lys
            180                 185                 190
```

<210> 184
<211> 2511
<212> DNA
<213> Homo sapiens

<400> 184
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cttttcacac tggccttaaa gaggatatat tagaagttga agtaggaagg gagccagaga 60
ggccgatggc gcaaaggtac gacgatctac cccattacgg gggcatggat ggagtaggca 120
tcccctccac gatgtatggg gacccgcatg cagccaggtc catgcagccg gtccaccacc 180
tgaaccacgg gcctcctctg cactcgcatc agtacccgca cacagctcat accaacgcca 240
tggcccccag catgggctcc tctgtcaatg acgctttaaa gagagataaa gatgccattt 300
atggacaccc cctcttccct ctcttagcac tgatttttga gaaatgtgaa ttagctactt 360
gtaccccccg cgagccgggg gtggcgggcg gggacgtctg ctcgtcagag tcattcaatg 420
aagatatagc cgtgttcgcc aaacagattc gcgcagaaaa acctctattt tcttctaatc 480
cagaactgga taacttgatg attcaagcca tacaagtatt aaggtttcat ctattggaat 540
tagagaaggt acacgaatta tgtgacaatt tctgccaccg gtatattagc tgtttgaaag 600
ggaaaatgcc tatcgatttg gtgatagacg atagagaagg aggatcaaaa tcagacagtg 660
aagatataac aagatcagca aatctaactg accagccctc ttggaacaga gatcatgatg 720
acacggcatc tactcgttca ggaggaaccc caggcccttc cagcggtggc cacacgtcac 780
acagtgggga caacagcagt gagcaaggtg atggcttgga caacagtgta gcttccccca 840
gcacaggtga cgatgatgac cctgataagg acaaaaagcg tcacaaaaag cgtggcatct 900
ttcccaaagt agccacaaat atcatgaggg cgtggctgtt ccagcatcta acacaccctt 960
acccttctga agaacagaaa aagcagttgg cacaagacac gggactcacc atccttcaag 1020
tgaacaattg gtttattaat gcccggagaa gaatagtgca gcccatgata gaccagtcca 1080
accgagcagt aagtcaagga acaccttata atcctgatgg acagcccatg ggaggtttcg 1140
taatggacgg tcagcaacat atgggaatta gagcaccagg acctatgagt ggaatgggca 1200
tgaatatggg catggagggg cagtggcact acatgtaacc ttcatctagt taaccaatcg 1260
caaagcaagg gggaaggctg caaagtatgc caggggagta tgtagcccgg ggtggtccaa 1320
tgggtgtgag tatgggacag ccaagttata cccaacccca gatgcccccc catcctgctc 1380
agctgcgtca tgggcccccc atgcatacgt acattcctgg acaccctcac cacccaacag 1440
tgatgatgca tggaggaccg ccccaccctg gaatgccaat gtcagcatca agccccacag 1500
ttcttaatac aggagaccca acaatgagtg gacaagtcat ggacattcat gctcagtagc 1560
ttaagggaat atgcattgtc tgcaatggtg actgatttca aatcatgttt tttctgcaat 1620
gactgtggag ttccattctt ggcatctact ctggaccaag gagcatccct aattcttcat 1680
agggaccttt aaaaagcagg aaataccaac tgaagtcaat ttgggggaca tgctaaataa 1740
ctatataaga cattaagaga acaaagagtg aaatattgta aatgctatta tactgttatc 1800
catattacgt tgtttcttat agatttttta aaaaaaatgt gaaatttttc cacactatgt 1860
gtgttgtttc catagctctt cacttcctcc agaagcctcc ttacattaaa aagccttaca 1920
gttatcctgc aagggacagg aaggtctgat ttgcaggatt tttagagcat taaaataact 1980
atcaggcaga agaatctttc ttctcgccta ggatttcagc catgcgcgcg ctctctctct 2040
ttctctctct tttcctctct ctccctcttt ctagcctggg gcttgaattt gcatgtctaa 2100
ttcatttact caccatattt gaattggcct gaacagatgt aaatcgggaa ggatgggaaa 2160
aactgcagtc atcaacaatg attaatcagc tgttgcaggc agtgtcttaa ggagactggt 2220
aggaggaggc atggaaacca aaaggccgtg tgtttagaag cctaattgtc acatcaagca 2280
tcattgtccc catgcaacaa ccaccacctt atacatcact tcctgtttta agcagctcta 2340
aaacatagac tgaagattta tttttaatat gttgacttta tttctgagca aagcatcggt 2400
catgtgtgta ttttttcata gtcccacctt ggagcattta tgtagacatt gtaaataaat 2460
tttgtgcaaa aaggactgga aaaatgaact gtattattgc aatttttttt t         2511
```

<210> 185
<211> 390
<212> PRT
<213> Homo sapiens

<400> 185
Met Ala Gln Arg Tyr Asp Asp Leu Pro His Tyr Gly Gly Met Asp Gly

```
1               5                   10                  15
Val Gly Ile Pro Ser Thr Met Tyr Gly Asp Pro His Ala Ala Arg Ser
            20                  25                  30
Met Gln Pro Val His His Leu Asn His Gly Pro Pro Leu His Ser His
        35                  40                  45
Gln Tyr Pro His Thr Ala His Thr Asn Ala Met Ala Pro Ser Met Gly
    50                  55                  60
Ser Ser Val Asn Asp Ala Leu Lys Arg Asp Lys Asp Ala Ile Tyr Gly
65                  70                  75                  80
His Pro Leu Phe Pro Leu Leu Ala Leu Ile Phe Glu Lys Cys Glu Leu
                85                  90                  95
Ala Thr Cys Thr Pro Arg Glu Pro Gly Val Ala Gly Gly Asp Val Cys
            100                 105                 110
Ser Ser Glu Ser Phe Asn Glu Asp Ile Ala Val Phe Ala Lys Gln Ile
        115                 120                 125
Arg Ala Glu Lys Pro Leu Phe Ser Ser Asn Pro Glu Leu Asp Asn Leu
    130                 135                 140
Met Ile Gln Ala Ile Gln Val Leu Arg Phe His Leu Leu Glu Leu Glu
145                 150                 155                 160
Lys Val His Glu Leu Cys Asp Asn Phe Cys His Arg Tyr Ile Ser Cys
                165                 170                 175
Leu Lys Gly Lys Met Pro Ile Asp Leu Val Ile Asp Asp Arg Glu Gly
            180                 185                 190
Gly Ser Lys Ser Asp Ser Glu Asp Ile Thr Arg Ser Ala Asn Leu Thr
        195                 200                 205
Asp Gln Pro Ser Trp Asn Arg Asp His Asp Asp Thr Ala Ser Thr Arg
    210                 215                 220
Ser Gly Gly Thr Pro Gly Pro Ser Ser Gly Gly His Thr Ser His Ser
225                 230                 235                 240
Gly Asp Asn Ser Ser Glu Gln Gly Asp Gly Leu Asp Asn Ser Val Ala
                245                 250                 255
Ser Pro Ser Thr Gly Asp Asp Asp Asp Pro Asp Lys Asp Lys Lys Arg
            260                 265                 270
His Lys Lys Arg Gly Ile Phe Pro Lys Val Ala Thr Asn Ile Met Arg
        275                 280                 285
Ala Trp Leu Phe Gln His Leu Thr His Pro Tyr Pro Ser Glu Glu Gln
    290                 295                 300
Lys Lys Gln Leu Ala Gln Asp Thr Gly Leu Thr Ile Leu Gln Val Asn
305                 310                 315                 320
Asn Trp Phe Ile Asn Ala Arg Arg Arg Ile Val Gln Pro Met Ile Asp
                325                 330                 335
Gln Ser Asn Arg Ala Val Ser Gln Gly Thr Pro Tyr Asn Pro Asp Gly
            340                 345                 350
Gln Pro Met Gly Gly Phe Val Met Asp Gly Gln Gln His Met Gly Ile
        355                 360                 365
Arg Ala Pro Gly Pro Met Ser Gly Met Gly Met Asn Met Gly Met Glu
    370                 375                 380
Gly Gln Trp His Tyr Met
385                 390
```

<210> 186
<211> 517
<212> DNA
<213> Homo sapiens

<400> 186
cctccacagc aacttccttg atccctgcca cgcacgactg aacacagaca gcagccgcct 60

cgccatgaag ctgctgatgg tcctcatgct ggcggccctc ctcctgcact gctatgcaga 120
ttctggctgc aaactcctgg aggacatggt tgaaaagacc atcaattccg acatatctat 180
acctgaatac aaagagcttc ttcaagagtt catagacagt gatgccgctg cagaggctat 240
ggggaaattc aagcagtgtt tcctcaacca gtcacataga actctgaaaa actttggact 300
gatgatgcat acagtgtacg acagcatttg gtgtaatatg aagagtaatt aactttaccc 360
aaggcgtttg gctcagaggg ctacagacta tggccagaac tcatctgttg attgctagaa 420
accacttttc tttcttgtgt tgtcttttta tgtggaaact gctagacaac tgttgaaacc 480
tcaaattcat ttccatttca ataactaact gcaaatc 517

<210> 187
<211> 95
<212> PRT
<213> Homo sapiens

<400> 187
Met Lys Leu Leu Met Val Leu Met Leu Ala Ala Leu Leu Leu His Cys
1 5 10 15
Tyr Ala Asp Ser Gly Cys Lys Leu Leu Glu Asp Met Val Glu Lys Thr
20 25 30
Ile Asn Ser Asp Ile Ser Ile Pro Glu Tyr Lys Glu Leu Leu Gln Glu
35 40 45
Phe Ile Asp Ser Asp Ala Ala Ala Glu Ala Met Gly Lys Phe Lys Gln
50 55 60
Cys Phe Leu Asn Gln Ser His Arg Thr Leu Lys Asn Phe Gly Leu Met
65 70 75 80
Met His Thr Val Tyr Asp Ser Ile Trp Cys Asn Met Lys Ser Asn
85 90 95

<210> 188
<211> 2048
<212> DNA
<213> Homo sapiens

<400> 188
ctctgcaaca gccgcgcttc ccgggtcccg cggctcccgc gcgcgatctg ccgcggccgg 60
ctgctgggca aaaatcagag ccgcctccgc cccattaccc atcatggaaa ccctccagga 120
aaaagtggcc ccggacgcgc gagcctgagg attctgcaca aaagaggtgc ccaaaatgaa 180
gaccctgatg cgccatggtc tggcagtgtg tttagcgctc accaccatgt gcaccagctt 240
gttgctagtg tacagcagcc tcggcggcca gaaggagcgg cccccgcagc agcagcagca 300
gcagcagcaa cagcagcagc aggcgtcggc caccggcagc tcgcagccgg cggcggagag 360
cagcacccag cagcgccccg gggtccccgc gggaccgcgg ccactggacg gatacctcgg 420
agtggcggac cacaagcccc tgaaaatgca ctgcagggac tgtgccctgg tgaccagctc 480
agggcatctg ctgcacagtc ggcaaggctc ccagattgac cagacagagt gtgtcatccg 540
catgaatgac gcccccacac gcggctatgg gcgtgacgtg ggcaatcgca ccagcctgag 600
ggtcatcgcg cattccagca tccagaggat cctccgcaac cgccatgacc tgctcaacgt 660
gagccagggc accgtgttca tcttctgggg ccccagcagc tacatgcggc gggacggcaa 720
gggccaggtc tacaacaacc tgcatctcct gagccaggtg ctgccccggc tgaaggcctt 780
catgattact cgccacaaga tgctgcagtt tgatgagctc ttcaagcagg agactggcaa 840
agacaggaag atatccaaca cttggctcag cactggctgg tttacaatga caattgcact 900
ggagctctgt gacaggatca atgtttatgg catggtgccc ccagacttct gcagggatcc 960
caatcacccc tcagtacctt atcattatta tgaacctttt ggacctgatg aatgtacaat 1020
gtacctctcc catgagcgag gacgcaaggg cagtcatcac cgctttatca cagagaaacg 1080
agtctttaag aactgggcac ggacattcaa tattcacttt tttcaaccag actggaaacc 1140
agaatcactt gctataaatc atcctgagaa taaacctgtg ttctaaggaa tgagcatgcc 1200
agactgtaat cccaggtatt cactgcatca gacaccgaga cactgaactt cctgagccac 1260
cagacaggaa agggtagcag aaaacagctt cactcctcag gaagtaccat ggacagacgc 1320
ctaccagggg tgacaaagca gtgcagttgg attgtaagga aaaattccgg aattaatgca 1380

tcctaatgaa tgttgtcccc ttcaatggtg ttaccttagg agctgaacat tcaattcagt 1440
tacaccacta tgactaaaaa cagtttggat ctcttagtat tgcctttgaa actgcaacat 1500
aagcaactca acaatattag ttgcattcct ttatagacat accatgtcaa agacgttttt 1560
ctatcaagtt gtattctttc ctgttctata acctttgtca tctgttagac tctgtatgtg 1620
tgatttgtaa aaagcaggct gaaactatgg acatgatttc tgaagagcac atctccactg 1680
actttcataa agcaaatgtc caatatttat ttattgagag tttttagtg caatctgggc 1740
cagtattttt atagattatg attatgtggt aatttatcct tcctaactct ttaatcctga 1800
atgatggttg gaaatggcct agaattaggt tactctgttc acaatgctca ttgttagcat 1860
gcaattggta tttgacttgg aagtgttgtg ttgtattttt tgaaccccta ggcttcagga 1920
aaactgctct tttgtaaaaa gaatagcgat gacattttct aatgtgcaga aatgttccaa 1980
aaggacaaaa ttgaaaacca aaaactatgt tattaaaaca aaaaaatgct aaaaaaaaaa 2040
aaaaaaaa 2048

<210> 189
<211> 336
<212> PRT
<213> Homo sapiens

<400> 189
Met Lys Thr Leu Met Arg His Gly Leu Ala Val Cys Leu Ala Leu Thr
1 5 10 15
Thr Met Cys Thr Ser Leu Leu Leu Val Tyr Ser Ser Leu Gly Gly Gln
20 25 30
Lys Glu Arg Pro Pro Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln
35 40 45
Gln Ala Ser Ala Thr Gly Ser Ser Gln Pro Ala Ala Glu Ser Ser Thr
50 55 60
Gln Gln Arg Pro Gly Val Pro Ala Gly Pro Arg Pro Leu Asp Gly Tyr
65 70 75 80
Leu Gly Val Ala Asp His Lys Pro Leu Lys Met His Cys Arg Asp Cys
85 90 95
Ala Leu Val Thr Ser Ser Gly His Leu Leu His Ser Arg Gln Gly Ser
100 105 110
Gln Ile Asp Gln Thr Glu Cys Val Ile Arg Met Asn Asp Ala Pro Thr
115 120 125
Arg Gly Tyr Gly Arg Asp Val Gly Asn Arg Thr Ser Leu Arg Val Ile
130 135 140
Ala His Ser Ser Ile Gln Arg Ile Leu Arg Asn Arg His Asp Leu Leu
145 150 155 160
Asn Val Ser Gln Gly Thr Val Phe Ile Phe Trp Gly Pro Ser Ser Tyr
165 170 175
Met Arg Arg Asp Gly Lys Gly Gln Val Tyr Asn Asn Leu His Leu Leu
180 185 190
Ser Gln Val Leu Pro Arg Leu Lys Ala Phe Met Ile Thr Arg His Lys
195 200 205
Met Leu Gln Phe Asp Glu Leu Phe Lys Gln Glu Thr Gly Lys Asp Arg
210 215 220
Lys Ile Ser Asn Thr Trp Leu Ser Thr Gly Trp Phe Thr Met Thr Ile
225 230 235 240
Ala Leu Glu Leu Cys Asp Arg Ile Asn Val Tyr Gly Met Val Pro Pro
245 250 255
Asp Phe Cys Arg Asp Pro Asn His Pro Ser Val Pro Tyr His Tyr Tyr
260 265 270
Glu Pro Phe Gly Pro Asp Glu Cys Thr Met Tyr Leu Ser His Glu Arg
275 280 285
Gly Arg Lys Gly Ser His His Arg Phe Ile Thr Glu Lys Arg Val Phe
290 295 300
Lys Asn Trp Ala Arg Thr Phe Asn Ile His Phe Phe Gln Pro Asp Trp

305 310 315 320
Lys Pro Glu Ser Leu Ala Ile Asn His Pro Glu Asn Lys Pro Val Phe
325 330 335

<210> 190
<211> 1078
<212> DNA
<213> Homo sapiens

<400> 190
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tgggaacagg ctcaggacta tctcaagaga ttttatctct atgactcaga aacaaaaaat 180
gccaacagtt tagaagccaa actcaaggag atgcaaaaat tctttggcct acctataact 240
ggaatgttaa actcccgcgt catagaaata atgcagaagc ccagatgtgg agtgccagat 300
gttgcagaat actcactatt tccaaatagc ccaaaatgga cttccaaagt ggtcacctac 360
aggatcgtat catatactcg agacttaccg catattacag tggatcgatt agtgtcaaag 420
gctttaaaca tgtggggcaa agagatcccc ctgcatttca ggaaagttgt atggggaact 480
gctgacatca tgattggctt tgcgcgagga gctcatgggg actcctaccc atttgatggg 540
ccaggaaaca cgctggctca tgcctttgcg cctgggacag gtctcggagg agatgctcac 600
ttcgatgagg atgaacgctg gacggatggt agcagtctag ggattaactt cctgtatgct 660
gcaactcatg aacttggcca ttctttgggt atgggacatt cctctgatcc taatgcagtg 720
atgtatccaa cctatggaaa tggagatccc caaaatttta aactttccca ggatgatatt 780
aaaggcattc agaaactata tggaaagaga agtaattcaa gaaagaaata gaaacttcag 840
gcagaacatc cattcattca ttcattggat tgtatatcat tgttgcacaa tcagaattga 900
taagcactgt tcctccactc catttagcaa ttatgtcacc ctttttttatt gcagttggtt 960
tttgaatgtc tttcactcct tttattggtt aaactccttt atggtgtgac tgtgtcttat 1020
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<210> 191
<211> 267
<212> PRT
<213> Homo sapiens

<400> 191
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Ala Leu Pro Leu Pro Gln Glu Ala Gly Gly Met Ser Glu Leu Gln Trp
20 25 30
Glu Gln Ala Gln Asp Tyr Leu Lys Arg Phe Tyr Leu Tyr Asp Ser Glu
35 40 45
Thr Lys Asn Ala Asn Ser Leu Glu Ala Lys Leu Lys Glu Met Gln Lys
50 55 60
Phe Phe Gly Leu Pro Ile Thr Gly Met Leu Asn Ser Arg Val Ile Glu
65 70 75 80
Ile Met Gln Lys Pro Arg Cys Gly Val Pro Asp Val Ala Glu Tyr Ser
85 90 95
Leu Phe Pro Asn Ser Pro Lys Trp Thr Ser Lys Val Val Thr Tyr Arg
100 105 110
Ile Val Ser Tyr Thr Arg Asp Leu Pro His Ile Thr Val Asp Arg Leu
115 120 125
Val Ser Lys Ala Leu Asn Met Trp Gly Lys Glu Ile Pro Leu His Phe
130 135 140
Arg Lys Val Val Trp Gly Thr Ala Asp Ile Met Ile Gly Phe Ala Arg
145 150 155 160
Gly Ala His Gly Asp Ser Tyr Pro Phe Asp Gly Pro Gly Asn Thr Leu
165 170 175

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Ala His Ala Phe Ala Pro Gly Thr Gly Leu Gly Gly Asp Ala His Phe
            180                 185                 190
Asp Glu Asp Glu Arg Trp Thr Asp Gly Ser Ser Leu Gly Ile Asn Phe
        195                 200                 205
Leu Tyr Ala Ala Thr His Glu Leu Gly His Ser Leu Gly Met Gly His
    210                 215                 220
Ser Ser Asp Pro Asn Ala Val Met Tyr Pro Thr Tyr Gly Asn Gly Asp
225                 230                 235                 240
Pro Gln Asn Phe Lys Leu Ser Gln Asp Asp Ile Lys Gly Ile Gln Lys
                245                 250                 255
Leu Tyr Gly Lys Arg Ser Asn Ser Arg Lys Lys
            260                 265


<210> 192
<211> 2217
<212> DNA
<213> Homo sapiens

<400> 192
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tcctgtggga cccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcacccct ggacggagtc 240
ctggccaacc cacctaacat ttccagcctc tcccctcgcc aactccttgg cttcccgtgt 300
gcggaggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360
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cccgaggacc tggacgccct cccattggac ctgctgctat tcctcaaccc agatgcgttc 480
tcggggcccc aggcctgcac ccgtttcttc tcccgcatca cgaaggccaa tgtggacctg 540
ctcccgaggg gggctcccga gcgacagcgg ctgctgcctg cggctctggc ctgctggggt 600
gtgcgggggt ctctgctgag cgaggctgat gtgcgggctc tgggaggcct ggcttgcgac 660
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ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780
ccccccctacg gcccccgtc gacatggtct gtctccacga tggacgctct gcggggcctg 840
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cggttccggc gggaagtgga gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020
gacgagagcc tcatcttcta caagaagtgg gagctggaag cctgcgtgga tgcggccctg 1080
ctggccaccc agatggaccg cgtgaacgcc atccccttca cctacgagca gctggacgtc 1140
ctaaagcata aactggatga gctctaccca caaggttacc ccgagtctgt gatccagcac 1200
ctgggctacc tcttcctcaa gatgagccct gaggacattc gcaagtggaa tgtgacgtcc 1260
ctggagaccc tgaaggcttt gcttgaagtc aacaaagggc acgaaatgag tcctcaggct 1320
cctcggcggc ccctcccaca ggtggccacc ctgatcgacc gctttgtgaa gggaaggggc 1380
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gacctggaca cgtgtgaccc aaggcagctg gacgtcctct atcccaaggc ccgccttgct 1560
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cccacggagg atttgaaggc gctcagtcag cagaatgtga gcatggactt ggccacgttc 1680
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cctagcctcc accctggcct gagggcccca ctcccttgct ggccccagcc ctgctgggga 2100
tccccgcctg gccaggagca ggcacgggtg atccccgttc caccccaaga gaactcgcgc 2160
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<210> 193
<211> 702
<212> PRT
<213> Homo sapiens

<400> 193
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Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20 25 30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35 40 45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50 55 60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65 70 75 80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85 90 95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100 105 110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115 120 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130 135 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145 150 155 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165 170 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180 185 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195 200 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210 215 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225 230 235 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
245 250 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
260 265 270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
275 280 285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
290 295 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305 310 315 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
325 330 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
340 345 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
355 360 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
370 375 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385 390 395 400
Val Asn Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu
405 410 415

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Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
            420                 425                 430
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
        435                 440                 445
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
    450                 455                 460
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
465                 470                 475                 480
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
                485                 490                 495
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
            500                 505                 510
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
        515                 520                 525
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
    530                 535                 540
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
545                 550                 555                 560
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
                565                 570                 575
Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
            580                 585                 590
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Gly Arg Gly Gly Gln
        595                 600                 605
Ala Arg Ala Gly Gly Arg Ala Gly Gly Val Glu Val Gly Ala Leu Ser
    610                 615                 620
His Pro Ser Leu Cys Arg Gly Pro Leu Gly Asp Ala Leu Pro Pro Arg
625                 630                 635                 640
Thr Trp Thr Cys Ser His Arg Pro Gly Thr Ala Pro Ser Leu His Pro
                645                 650                 655
Gly Leu Arg Ala Pro Leu Pro Cys Trp Pro Gln Pro Cys Trp Gly Ser
            660                 665                 670
Pro Pro Gly Gln Glu Gln Ala Arg Val Ile Pro Val Pro Pro Gln Glu
        675                 680                 685
Asn Ser Arg Ser Val Asn Gly Asn Met Pro Pro Ala Asp Thr
    690                 695                 700
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<210> 194
<211> 2135
<212> DNA
<213> Homo sapiens

<400> 194

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tcctgtggga cccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcacccct ggacggagtc 240
ctggccaacc cacctaacat ttccagcctc tcccctcgcc aactccttgg cttcccgtgt 300
gcggaggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360
aagaatgtca agctctcaac agagcagctg cgctgtctgg ctcaccggct ctctgagccc 420
cccgaggacc tggacgccct cccattggac ctgctgctat tcctcaaccc agatgcgttc 480
tcggggcccc aggcctgcac ccgtttcttc tcccgcatca cgaaggccaa tgtggacctg 540
ctcccgaggg gggctcccga gcgacagcgg ctgctgcctg cggctctggc ctgctggggt 600
gtgcgggggt ctctgctgag cgaggctgat gtgcgggctc tgggaggcct ggcttgcgac 660
ctgcctgggc gctttgtggc cgagtcggcc gaagtgctgc taccccggct ggtgagctgc 720
ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780
ccccccctacg gcccccccgtc gacatggtct gtctccacga tggacgctct gcggggcctg 840
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ctgcccgtgc tgggccagcc catcatccgc agcatcccgc agggcatcgt ggccgcgtgg 900
cggcaacgct cctctcggga cccatcctgg cggcagcctg aacggaccat cctccggccg 960
cggttccggc gggaagtgga gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020
gacgagagcc tcatcttcta caagaagtgg gagctggaag cctgcgtgga tgcggccctg 1080
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ctaaagcata aactggatga gctctaccca caaggttacc ccgagtctgt gatccagcac 1200
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ctggagaccc tgaaggcttt gcttgaagtc aacaaagggc acgaaatgag tcctcaggct 1320
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ctacggcagc ggcaggacga cctggacacg ctggggctgg ggctacaggg cggcatcccc 1860
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ctaggacctg gacctgttct caccgtcctg gcactgctcc tagcctccac cctggcctga 1980
gggccccact cccttgctgg ccccagccct gctggggatc cccgcctggc caggagcagg 2040
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ctgcagacac gtaaaaaaaa aaaaaaaaaa aaaaa                            2135
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<210> 195
<211> 630
<212> PRT
<213> Homo sapiens

<400> 195

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Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
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Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
            20                  25                  30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
        35                  40                  45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
    50                  55                  60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65                  70                  75                  80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
                85                  90                  95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
            100                 105                 110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
        115                 120                 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
    130                 135                 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145                 150                 155                 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
                165                 170                 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
            180                 185                 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
        195                 200                 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
    210                 215                 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
```

```
225                 230                 235                 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
                245                 250                 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
            260                 265                 270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
        275                 280                 285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
    290                 295                 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305                 310                 315                 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
                325                 330                 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
            340                 345                 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
        355                 360                 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
    370                 375                 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385                 390                 395                 400
Val Asn Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu
                405                 410                 415
Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
            420                 425                 430
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
        435                 440                 445
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
    450                 455                 460
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
465                 470                 475                 480
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
                485                 490                 495
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
            500                 505                 510
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
        515                 520                 525
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
    530                 535                 540
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
545                 550                 555                 560
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
                565                 570                 575
Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
            580                 585                 590
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Glu Ala Leu Ser Gly Thr
        595                 600                 605
Pro Cys Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu
    610                 615                 620
Leu Ala Ser Thr Leu Ala
625                 630
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<210> 196
<211> 2105
<212> DNA
<213> Homo sapiens

<400> 196
ggccggccac tcccgtctgc tgtgacgcgc ggacagagag ctaccggtgg acccacggtg 60
cctccctccc tgggatctac acagaccatg gccttgccaa cggctcgacc cctgttgggg 120
tcctgtggga cccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcaccccct ggacggagtc 240
ctggccaacc cacctaacat ttccagcctc tcccctcgcc aactccttgg cttcccgtgt 300
gcggaggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360
aagaatgtca agctctcaac agagcagctg cgctgtctgg ctcaccggct ctctgagccc 420
cccgaggacc tggacgccct cccattggac ctgctgctat tcctcaaccc agatgcgttc 480
tcggggcccc aggcctgcac ccgtttcttc tcccgcatca cgaaggccaa tgtggacctg 540
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ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780
ccccccctacg gccccccgtc gacatggtct gtctccacga tggacgctct gcggggcctg 840
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cggttccggc gggaagtgga gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020
gacgagagcc tcatcttcta caagaagtgg gagctggaag cctgcgtgga tgcggccctg 1080
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ctaaagcata aactggatga gctctaccca caaggttacc ccgagtctgt gatccagcac 1200
ctgggctacc tcttcctcaa gatgagccct gaggacattc gcaagtggaa tgtgacgtcc 1260
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gacctggaca cgtgtgaccc aaggcagctg gacgtcctct atcccaaggc ccgccttgct 1560
ttccagaaca tgaacgggtc cgaatacttc gtgaagatcc agtccttcct gggtggggcc 1620
cccacggagg atttgaaggc gctcagtcag cagaatgtga gcatggactt ggccacgttc 1680
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ctacggcagc ggcaggacga cctggacacg ctggggctgg ggctacaggg cggcatcccc 1860
aacggctacc tggtcctaga cctcagcgtg caaggacctg gacctgttct caccgtcctg 1920
gcactgctcc tagcctccac cctggcctga gggccccact ccccttgctgg ccccagccct 1980
gctggggatc cccgcctggc caggagcagg cacgggtgat ccccgttcca ccccaagaga 2040
actcgcgctc agtaaacggg aacatgcccc ctgcagacac gtaaaaaaaa aaaaaaaaaa 2100
aaaaa 2105

<210> 197
<211> 620
<212> PRT
<213> Homo sapiens

<400> 197
Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
1 5 10 15
Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20 25 30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35 40 45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50 55 60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65 70 75 80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85 90 95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100 105 110

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Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
        115                 120                 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
    130                 135                 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145                 150                 155                 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
                165                 170                 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
            180                 185                 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
        195                 200                 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
    210                 215                 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225                 230                 235                 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
                245                 250                 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
            260                 265                 270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
        275                 280                 285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
    290                 295                 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305                 310                 315                 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
                325                 330                 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
            340                 345                 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
        355                 360                 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
    370                 375                 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385                 390                 395                 400
Val Asn Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu
                405                 410                 415
Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
            420                 425                 430
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
        435                 440                 445
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
    450                 455                 460
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
465                 470                 475                 480
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
                485                 490                 495
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
            500                 505                 510
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
        515                 520                 525
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
    530                 535                 540
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
545                 550                 555                 560
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
                565                 570                 575
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Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
            580                 585                 590
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Pro Gly Pro Val Leu
        595                 600                 605
Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala
    610                 615                 620
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<210> 198
<211> 2193
<212> DNA
<213> Homo sapiens

<400> 198

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tcctgtggga cccccgccct cggcagcctc ctgttcctgc tcttcagcct cggatgggtg 180
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cccgaggacc tggacgccct cccattggac ctgctgctat tcctcaaccc agatgcgttc 480
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gtgcgggggt ctctgctgag cgaggctgat gtgcgggctc tgggaggcct ggcttgcgac 660
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ccgggacccc tggaccagga ccagcaggag gcagccaggg cggctctgca gggcggggga 780
ccccccctacg gcccccgtc gacatggtct gtctccacga tggacgctct gcggggcctg 840
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<210> 199
<211> 694
<212> PRT
<213> Homo sapiens

<400> 199

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Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
20 25 30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35 40 45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50 55 60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65 70 75 80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85 90 95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100 105 110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115 120 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130 135 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145 150 155 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165 170 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180 185 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195 200 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210 215 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225 230 235 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
245 250 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
260 265 270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
275 280 285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
290 295 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305 310 315 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
325 330 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
340 345 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
355 360 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
370 375 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385 390 395 400
Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp
405 410 415
Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr
420 425 430
Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu
435 440 445
Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp
450 455 460

Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala
465 470 475 480
Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile
485 490 495
Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser
500 505 510
Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr
515 520 525
Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly
530 535 540
Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg
545 550 555 560
Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu
565 570 575
Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser
580 585 590
Val Gln Gly Gly Arg Gly Gly Gln Ala Arg Ala Gly Gly Arg Ala Gly
595 600 605
Gly Val Glu Val Gly Ala Leu Ser His Pro Ser Leu Cys Arg Gly Pro
610 615 620
Leu Gly Asp Ala Leu Pro Pro Arg Thr Trp Thr Cys Ser His Arg Pro
625 630 635 640
Gly Thr Ala Pro Ser Leu His Pro Gly Leu Arg Ala Pro Leu Pro Cys
645 650 655
Trp Pro Gln Pro Cys Trp Gly Ser Pro Pro Gly Gln Glu Gln Ala Arg
660 665 670
Val Ile Pro Val Pro Pro Gln Glu Asn Ser Arg Ser Val Asn Gly Asn
675 680 685
Met Pro Pro Ala Asp Thr
690

<210> 200
<211> 2081
<212> DNA
<213> Homo sapiens

<400> 200
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cagccctcga ggaccctggc tggagagaca gggcaggagg ctgcacccct ggacggagtc 240
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gcggaggtgt ccggcctgag cacggagcgt gtccgggagc tggctgtggc cttggcacag 360
aagaatgtca agctctcaac agagcagctg cgctgtctgg ctcaccggct ctctgagccc 420
cccgaggacc tggacgccct cccattggac ctgctgctat tcctcaaccc agatgcgttc 480
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gtgcgggggt ctctgctgag cgaggctgat gtgcgggctc tgggaggcct ggcttgcgac 660
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ccccccctacg gcccccccgtc gacatggtct gtctccacga tggacgctct gcggggcctg 840
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cggttccggc gggaagtgga gaagacagcc tgtccttcag gcaagaaggc ccgcgagata 1020
gacgagagcc tcatcttcta caagaagtgg gagctggaag cctgcgtgga tgcggccctg 1080
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ctaaagcata aactggatga gctctaccca caaggttacc ccgagtctgt gatccagcac 1200

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gccaccctga tcgaccgctt tgtgaaggga aggggccagc tagacaaaga caccctagac 1380
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agtcagcaga atgtgagcat ggacttggcc acgttcatga agctgcggac ggatgcggtg 1680
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gcctgagggc cccactccct tgctggcccc agccctgctg gggatccccg cctggccagg 1980
agcaggcacg ggtgatcccc gttccacccc aagagaactc gcgctcagta aacgggaaca 2040
tgccccctgc agacacgtaa aaaaaaaaaa aaaaaaaaaa a                     2081

<210> 201
<211> 612
<212> PRT
<213> Homo sapiens

<400> 201
Met Ala Leu Pro Thr Ala Arg Pro Leu Leu Gly Ser Cys Gly Thr Pro
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Ala Leu Gly Ser Leu Leu Phe Leu Leu Phe Ser Leu Gly Trp Val Gln
            20                  25                  30
Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
        35                  40                  45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
    50                  55                  60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65                  70                  75                  80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
                85                  90                  95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
            100                 105                 110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
        115                 120                 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
    130                 135                 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145                 150                 155                 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
                165                 170                 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
            180                 185                 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
        195                 200                 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
    210                 215                 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225                 230                 235                 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
                245                 250                 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
            260                 265                 270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
        275                 280                 285
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Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
290 295 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305 310 315 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
325 330 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
340 345 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
355 360 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
370 375 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385 390 395 400
Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp
405 410 415
Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr
420 425 430
Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu
435 440 445
Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp
450 455 460
Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala
465 470 475 480
Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile
485 490 495
Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser
500 505 510
Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr
515 520 525
Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly
530 535 540
Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg
545 550 555 560
Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu
565 570 575
Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser
580 585 590
Val Gln Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu Leu Ala
595 600 605
Ser Thr Leu Ala
610

<210> 202
<211> 1195
<212> DNA
<213> Homo sapiens

<400> 202
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gaccgcgtga acgccatccc cttcacctac gagcagctgg acgtcctaaa gcataaactg 180
gatgagctct acccacaagg ttaccccgag tctgtgatcc agcacctggg ctacctcttc 240
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gctttgcttg aagtcaacaa agggcacgaa atgagtcctc aggtggccac cctgatcgac 360
cgctttgtga agggaagggg ccagctagac aaagacaccc tagacaccct gaccgccttc 420
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atctgggcgg tcaggcccca ggacctggac acgtgtgacc caaggcagct ggacgtcctc 540
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agcatggact tggccacgtt catgaagctg cggacggatg cggtgctgcc gttgactgtg 720
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<210> 203
<211> 398
<212> PRT
<213> Homo sapiens

<400> 203
Val Glu Lys Thr Ala Cys Pro Ser Gly Lys Lys Ala Arg Glu Ile Asp
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Glu Ser Leu Ile Phe Tyr Lys Lys Trp Glu Leu Glu Ala Cys Val Asp
20 25 30
Ala Ala Leu Leu Ala Thr Gln Met Asp Arg Val Asn Ala Ile Pro Phe
35 40 45
Thr Tyr Glu Gln Leu Asp Val Leu Lys His Lys Leu Asp Glu Leu Tyr
50 55 60
Pro Gln Gly Tyr Pro Glu Ser Val Ile Gln His Leu Gly Tyr Leu Phe
65 70 75 80
Leu Lys Met Ser Pro Glu Asp Ile Arg Lys Trp Asn Val Thr Ser Leu
85 90 95
Glu Thr Leu Lys Ala Leu Leu Glu Val Asn Lys Gly His Glu Met Ser
100 105 110
Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
115 120 125
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
130 135 140
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
145 150 155 160
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
165 170 175
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
180 185 190
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
195 200 205
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
210 215 220
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
225 230 235 240
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
245 250 255
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
260 265 270
Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
275 280 285
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Gly Gly Arg Gly Gly Gln
290 295 300
Ala Arg Ala Gly Gly Arg Ala Gly Gly Val Glu Val Gly Ala Leu Ser

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305                 310                 315                 320
His Pro Ser Leu Cys Arg Gly Pro Leu Gly Asp Ala Leu Pro Pro Arg
                325                 330                 335
Thr Trp Thr Cys Ser His Arg Pro Gly Thr Ala Pro Ser Leu His Pro
            340                 345                 350
Gly Leu Arg Ala Pro Leu Pro Cys Trp Pro Gln Pro Cys Trp Gly Ser
        355                 360                 365
Pro Pro Gly Gln Glu Gln Ala Arg Val Ile Pro Val Pro Pro Gln Glu
    370                 375                 380
Asn Ser Arg Ser Val Asn Gly Asn Met Pro Pro Ala Asp Thr
385                 390                 395
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<210> 204
<211> 2085
<212> DNA
<213> Homo sapiens

<400> 204

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tgtgggaccc ccgccctcgg cagcctcctg ttcctgctct tcagcctcgg atgggtgcag 180
ccctcgagga ccctggctgg agagacaggg caggaggctg cacccctgga cggagtcctg 240
gccaacccac ctaacatttc cagcctctcc cctcgccaac tccttggctt cccgtgtgcg 300
gaggtgtccg gcctgagcac ggagcgtgtc cgggagctgg ctgtggcctt ggcacagaag 360
aatgtcaagc tctcaacaga gcagctgcgc tgtctggctc accggctctc tgagcccccc 420
gaggacctgg acgccctccc attggacctg ctgctattcc tcaacccaga tgcgttctcg 480
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ggctacctct tcctcaagat gagccctgag gacattcgca agtggaatgt gacgtccctg 1260
gagaccctga aggctttgct tgaagtcaac aaagggcacg aaatgagtcc tcaggtggcc 1320
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cctgctgggg atccccgcct ggccaggagc aggcacgggt gatccccgtt ccaccccaag 2040
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<210> 205
<211> 622
<212> PRT

<213> Homo sapiens

<400> 205
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Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35 40 45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50 55 60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65 70 75 80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85 90 95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100 105 110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115 120 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130 135 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145 150 155 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165 170 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180 185 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195 200 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210 215 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225 230 235 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
245 250 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
260 265 270
Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
275 280 285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
290 295 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305 310 315 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
325 330 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
340 345 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
355 360 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
370 375 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385 390 395 400
Val Asn Lys Gly His Glu Met Ser Pro Gln Val Ala Thr Leu Ile Asp
405 410 415
Arg Phe Val Lys Gly Arg Gly Gln Leu Asp Lys Asp Thr Leu Asp Thr
420 425 430
Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys Ser Leu Ser Pro Glu Glu

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        435                 440                 445
Leu Ser Ser Val Pro Pro Ser Ser Ile Trp Ala Val Arg Pro Gln Asp
    450                 455                 460
Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp Val Leu Tyr Pro Lys Ala
465                 470                 475                 480
Arg Leu Ala Phe Gln Asn Met Asn Gly Ser Glu Tyr Phe Val Lys Ile
                485                 490                 495
Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu Asp Leu Lys Ala Leu Ser
            500                 505                 510
Gln Gln Asn Val Ser Met Asp Leu Ala Thr Phe Met Lys Leu Arg Thr
        515                 520                 525
Asp Ala Val Leu Pro Leu Thr Val Ala Glu Val Gln Lys Leu Leu Gly
    530                 535                 540
Pro His Val Glu Gly Leu Lys Ala Glu Glu Arg His Arg Pro Val Arg
545                 550                 555                 560
Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp Leu Asp Thr Leu Gly Leu
                565                 570                 575
Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr Leu Val Leu Asp Leu Ser
            580                 585                 590
Val Gln Glu Ala Leu Ser Gly Thr Pro Cys Leu Leu Gly Pro Gly Pro
        595                 600                 605
Val Leu Thr Val Leu Ala Leu Leu Leu Ala Ser Thr Leu Ala
    610                 615                 620
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<210> 206
<211> 2111
<212> DNA
<213> Homo sapiens

<400> 206

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agccctgctg gggatccccg cctggccagg agcaggcacg ggtgatcccc gttccacccc 2040
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aaaaaaaaaa a 2111

<210> 207
<211> 2107
<212> DNA
<213> Homo sapiens

<400> 207
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ctgtggggac cgccctggca gcctcctgtt cctgctcttc agcctcggat gggtgcatcc 180
cgcgaggacc ctggctggag agacagggac ggagtctgcc cccctggggg gagtcctgac 240
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<210> 208
<211> 628
<212> PRT
<213> Homo sapiens

<400> 208

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            20                  25                  30
Arg Thr Leu Ala Gly Glu Thr Gly Thr Glu Ser Ala Pro Leu Gly Gly
        35                  40                  45
Val Leu Thr Thr Pro His Asn Ile Ser Ser Leu Ser Pro Arg Gln Leu
    50                  55                  60
Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu Arg Val
65                  70                  75                  80
Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu Ser Thr
                85                  90                  95
Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro Glu Asp
            100                 105                 110
Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro Asp Ala
        115                 120                 125
Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile Thr Lys
    130                 135                 140
Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln Arg Leu
145                 150                 155                 160
Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu Leu Ser
                165                 170                 175
Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu Pro Gly
            180                 185                 190
Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu Val Ser
        195                 200                 205
Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg Ala Ala
    210                 215                 220
Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp Ser Val
225                 230                 235                 240
Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly Gln Pro
                245                 250                 255
Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg Gln Arg
            260                 265                 270
Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile Leu Arg
        275                 280                 285
Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser Gly Lys
    290                 295                 300
Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys Trp Glu
305                 310                 315                 320
Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met Asp Arg
                325                 330                 335
Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu Lys His
            340                 345                 350
Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val Ile Gln
        355                 360                 365
His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile Arg Lys
    370                 375                 380
Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu Val Asp
385                 390                 395                 400
Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu Pro Gln
                405                 410                 415
Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln Leu Asp
            420                 425                 430
Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr Leu Cys
        435                 440                 445
Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser Ile Trp
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    450                 455                 460
Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln Leu Asp
465                 470                 475                 480
Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn Gly Ser
                485                 490                 495
Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro Thr Glu
            500                 505                 510
Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu Ala Thr
        515                 520                 525
Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val Ala Glu
    530                 535                 540
Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala Glu Glu
545                 550                 555                 560
Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln Asp Asp
                565                 570                 575
Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn Gly Tyr
            580                 585                 590
Leu Val Leu Asp Leu Ser Val Gln Glu Thr Leu Ser Gly Thr Pro Cys
        595                 600                 605
Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu Leu Ala
    610                 615                 620
Ser Thr Leu Ala
625
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<210> 209
<211> 2316
<212> DNA
<213> Homo sapiens

<400> 209
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<210> 210
<211> 630
<212> PRT
<213> Homo sapiens

<220>
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<222> (1)...(630)
<223> Xaa = Any Amino Acid

<400> 210
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Pro Ser Arg Thr Leu Ala Gly Glu Thr Gly Gln Glu Ala Ala Pro Leu
35 40 45
Asp Gly Val Leu Ala Asn Pro Pro Asn Ile Ser Ser Leu Ser Pro Arg
50 55 60
Gln Leu Leu Gly Phe Pro Cys Ala Glu Val Ser Gly Leu Ser Thr Glu
65 70 75 80
Arg Val Arg Glu Leu Ala Val Ala Leu Ala Gln Lys Asn Val Lys Leu
85 90 95
Ser Thr Glu Gln Leu Arg Cys Leu Ala His Arg Leu Ser Glu Pro Pro
100 105 110
Glu Asp Leu Asp Ala Leu Pro Leu Asp Leu Leu Leu Phe Leu Asn Pro
115 120 125
Asp Ala Phe Ser Gly Pro Gln Ala Cys Thr Arg Phe Phe Ser Arg Ile
130 135 140
Thr Lys Ala Asn Val Asp Leu Leu Pro Arg Gly Ala Pro Glu Arg Gln
145 150 155 160
Arg Leu Leu Pro Ala Ala Leu Ala Cys Trp Gly Val Arg Gly Ser Leu
165 170 175
Leu Ser Glu Ala Asp Val Arg Ala Leu Gly Gly Leu Ala Cys Asp Leu
180 185 190
Pro Gly Arg Phe Val Ala Glu Ser Ala Glu Val Leu Leu Pro Arg Leu
195 200 205
Val Ser Cys Pro Gly Pro Leu Asp Gln Asp Gln Gln Glu Ala Ala Arg
210 215 220
Ala Ala Leu Gln Gly Gly Gly Pro Pro Tyr Gly Pro Pro Ser Thr Trp
225 230 235 240
Ser Val Ser Thr Met Asp Ala Leu Arg Gly Leu Leu Pro Val Leu Gly
245 250 255
Gln Pro Ile Ile Arg Ser Ile Pro Gln Gly Ile Val Ala Ala Trp Arg
260 265 270

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Gln Arg Ser Ser Arg Asp Pro Ser Trp Arg Gln Pro Glu Arg Thr Ile
        275                 280                 285
Leu Arg Pro Arg Phe Arg Arg Glu Val Glu Lys Thr Ala Cys Pro Ser
    290                 295                 300
Gly Lys Lys Ala Arg Glu Ile Asp Glu Ser Leu Ile Phe Tyr Lys Lys
305                 310                 315                 320
Trp Glu Leu Glu Ala Cys Val Asp Ala Ala Leu Leu Ala Thr Gln Met
                325                 330                 335
Asp Arg Val Asn Ala Ile Pro Phe Thr Tyr Glu Gln Leu Asp Val Leu
            340                 345                 350
Lys His Lys Leu Asp Glu Leu Tyr Pro Gln Gly Tyr Pro Glu Ser Val
        355                 360                 365
Ile Gln His Leu Gly Tyr Leu Phe Leu Lys Met Ser Pro Glu Asp Ile
    370                 375                 380
Arg Lys Trp Asn Val Thr Ser Leu Glu Thr Leu Lys Ala Leu Leu Glu
385                 390                 395                 400
Val Asp Lys Gly His Glu Met Ser Pro Gln Ala Pro Arg Arg Pro Leu
                405                 410                 415
Pro Gln Val Ala Thr Leu Ile Asp Arg Phe Val Lys Gly Arg Gly Gln
            420                 425                 430
Leu Asp Lys Asp Thr Leu Asp Thr Leu Thr Ala Phe Tyr Pro Gly Tyr
        435                 440                 445
Leu Cys Ser Leu Ser Pro Glu Glu Leu Ser Ser Val Pro Pro Ser Ser
    450                 455                 460
Ile Trp Ala Val Arg Pro Gln Asp Leu Asp Thr Cys Asp Pro Arg Gln
465                 470                 475                 480
Leu Asp Val Leu Tyr Pro Lys Ala Arg Leu Ala Phe Gln Asn Met Asn
                485                 490                 495
Gly Ser Glu Tyr Phe Val Lys Ile Gln Ser Phe Leu Gly Gly Ala Pro
            500                 505                 510
Thr Glu Asp Leu Lys Ala Leu Ser Gln Gln Asn Val Ser Met Asp Leu
        515                 520                 525
Ala Thr Phe Met Lys Leu Arg Thr Asp Ala Val Leu Pro Leu Thr Val
    530                 535                 540
Ala Glu Val Gln Lys Leu Leu Gly Pro His Val Glu Gly Leu Lys Ala
545                 550                 555                 560
Glu Glu Arg His Arg Pro Val Arg Asp Trp Ile Leu Arg Gln Arg Gln
                565                 570                 575
Asp Asp Leu Asp Thr Leu Gly Leu Gly Leu Gln Gly Gly Ile Pro Asn
            580                 585                 590
Gly Tyr Leu Val Leu Asp Leu Ser Val Gln Xaa Xaa Leu Ser Gly Thr
        595                 600                 605
Pro Cys Leu Leu Gly Pro Gly Pro Val Leu Thr Val Leu Ala Leu Leu
    610                 615                 620
Leu Ala Ser Thr Leu Ala
625                 630
```

<210> 211
<211> 1721
<212> DNA
<213> Homo sapiens

<400> 211
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acaggttctg gtcatgcaag ctctacccca ggtggagaaa aggagacttc ggctacccag 180
agaagttcag tgcccagctc tactgagaag aatgctgtga gtatgaccag cagcgtactc 240
```

```
tccagccaca gccccggttc aggctcctcc accactcagg gacaggatgt cactctggcc 300
ccggccacgg aaccagcttc aggttcagct gccacctggg gacaggatgt cacctcggtc 360
ccagtcacca ggccagccct gggctccacc accccgccag cccacgatgt cacctcagcc 420
ccggacaaca agccagcccc gggctccacc gcccccccag cccacggtgt cacctcggcc 480
ccggacacca ggccgccccc gggctccacc gcccccccag cccacggtgt cacctcggcc 540
ccggacacca ggccgccccc gggctccacc gcgcccgcag cccacggtgt cacctcggcc 600
ccggacacca ggccggcccc gggctccacc gcccccccag cccatggtgt cacctcggcc 660
ccggacaaca ggcccgcctt ggcgtccacc gcccctccag tccacaatgt cacctcggcc 720
tcaggctctg catcaggctc agcttctact ctggtgcaca acggcacctc tgccagggct 780
accacaaccc cagccagcaa gagcactcca ttctcaattc ccagccacca ctctgatact 840
cctaccaccc ttgccagcca tagcaccaag actgatgcca gtagcactca ccatagcacg 900
gtacctcctc tcacctcctc caatcacagc acttctcccc agttgtctac tggggtctct 960
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agcaccgact actaccaaga gctgcagaga gacatttctg aaatgttttt gcagatttat 1080
aaacaagggg gttttctggg cctctccaat attaagttca ggccaggatc tgtggtggta 1140
caattgactc tggccttccg agaaggtacc atcaatgtcc acgacgtgga gacacagttc 1200
aatcagtata aaacggaagc agcctctcga tataacctga cgatctcaga cgtcagcgtg 1260
agtgatgtgc catttccttt ctctgcccag tctggggctg gggtgccagg ctggggcatc 1320
gcgctgctgg tgctggtctg tgttctggtt gcgctggcca ttgtctatct cattgccttg 1380
gctgtctgtc agtgccgccg aaagaactac gggcagctgg acatctttcc agcccgggat 1440
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agcagtaccg atcgtagccc ctatgagaag gtttctgcag gtaatggtgg cagcagcctc 1560
tcttacacaa acccagcagt ggcagccact tctgccaact tgtaggggca cgtcgccctc 1620
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```

<210> 212
<211> 515
<212> PRT
<213> Homo sapiens

<400> 212

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Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu Leu Leu Leu Leu Thr
 1               5                  10                  15
Val Leu Thr Val Val Thr Gly Ser Gly His Ala Ser Ser Thr Pro Gly
            20                  25                  30
Gly Glu Lys Glu Thr Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser
        35                  40                  45
Thr Glu Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser His
    50                  55                  60
Ser Pro Gly Ser Gly Ser Ser Thr Thr Gln Gly Gln Asp Val Thr Leu
65                  70                  75                  80
Ala Pro Ala Thr Glu Pro Ala Ser Gly Ser Ala Ala Thr Trp Gly Gln
                85                  90                  95
Asp Val Thr Ser Val Pro Val Thr Arg Pro Ala Leu Gly Ser Thr Thr
            100                 105                 110
Pro Pro Ala His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala Pro
        115                 120                 125
Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    130                 135                 140
Arg Pro Pro Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
145                 150                 155                 160
Ala Pro Asp Thr Arg Pro Pro Pro Gly Ser Thr Ala Pro Ala Ala His
                165                 170                 175
Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            180                 185                 190
Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Asn Arg Pro Ala Leu
        195                 200                 205
```

```
Ala Ser Thr Ala Pro Pro Val His Asn Val Thr Ser Ala Ser Gly Ser
    210                 215                 220
Ala Ser Gly Ser Ala Ser Thr Leu Val His Asn Gly Thr Ser Ala Arg
225                 230                 235                 240
Ala Thr Thr Thr Pro Ala Ser Lys Ser Thr Pro Phe Ser Ile Pro Ser
                245                 250                 255
His His Ser Asp Thr Pro Thr Thr Leu Ala Ser His Ser Thr Lys Thr
            260                 265                 270
Asp Ala Ser Ser Thr His His Ser Thr Val Pro Pro Leu Thr Ser Ser
        275                 280                 285
Asn His Ser Thr Ser Pro Gln Leu Ser Thr Gly Val Ser Phe Phe Phe
    290                 295                 300
Leu Ser Phe His Ile Ser Asn Leu Gln Phe Asn Ser Ser Leu Glu Asp
305                 310                 315                 320
Pro Ser Thr Asp Tyr Tyr Gln Glu Leu Gln Arg Asp Ile Ser Glu Met
                325                 330                 335
Phe Leu Gln Ile Tyr Lys Gln Gly Gly Phe Leu Gly Leu Ser Asn Ile
            340                 345                 350
Lys Phe Arg Pro Gly Ser Val Val Val Gln Leu Thr Leu Ala Phe Arg
        355                 360                 365
Glu Gly Thr Ile Asn Val His Asp Val Glu Thr Gln Phe Asn Gln Tyr
    370                 375                 380
Lys Thr Glu Ala Ala Ser Arg Tyr Asn Leu Thr Ile Ser Asp Val Ser
385                 390                 395                 400
Val Ser Asp Val Pro Phe Pro Phe Ser Ala Gln Ser Gly Ala Gly Val
                405                 410                 415
Pro Gly Trp Gly Ile Ala Leu Leu Val Leu Val Cys Val Leu Val Ala
            420                 425                 430
Leu Ala Ile Val Tyr Leu Ile Ala Leu Ala Val Cys Gln Cys Arg Arg
        435                 440                 445
Lys Asn Tyr Gly Gln Leu Asp Ile Phe Pro Ala Arg Asp Thr Tyr His
    450                 455                 460
Pro Met Ser Glu Tyr Pro Thr Tyr His Thr His Gly Arg Tyr Val Pro
465                 470                 475                 480
Pro Ser Ser Thr Asp Arg Ser Pro Tyr Glu Lys Val Ser Ala Gly Asn
                485                 490                 495
Gly Gly Ser Ser Leu Ser Tyr Thr Asn Pro Ala Val Ala Ala Thr Ser
            500                 505                 510
Ala Asn Leu
        515
```

<210> 213
<211> 5793
<212> DNA
<213> Homo sapiens

<400> 213

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agctctgtgc caaccaccag cactcctggg acctccacag tgcacctggc aacctctggg 180
actccatcct ccctgcctgg ccacacagcc cctgtccctc tcttgatacc attcaccctc 240
aactttacca tcaccaacct gcattatgaa gaaaacatgc aacaccctgg ttccaggaag 300
ttcaacacca cggagagggt tctgcagggt ctgctcaagc ccttgttcaa gagcaccagc 360
gttggccctc tgtactctgg ctgcagactg accttgctca gacctgagaa acatggggca 420
gccactggag tggacgccat ctgcaccctc cgccttgatc ccactggtcc tggactggac 480
agagagcggc tatactggga gctgagccag ctgaccaaca gcgttacaga gctgggcccc 540
tacaccctgg acagggacag tctctatgtc aatggcttca cccatcggag ctctgtgcca 600
```

accaccagta ttcctgggac ctctgcagtg cacctggaaa cctctgggac tccagcctcc 660
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accaacctgc agtatgagga ggacatgcgt caccctggtt ccaggaagtt caacaccacg 780
gagagagtcc tgcagggtct gctcaagccc ttgttcaaga gcaccagtgt tggccctctg 840
tactctggct gcagactgac cttgctcagg cctgaaaaac gtggggcagc caccggcgtg 900
gacaccatct gcactcaccg ccttgaccct ctaaaccctg gactggacag agagcagcta 960
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaa                             5793
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<210> 214
<211> 1783
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> (1)...(1783)
<223> Xaa = Any Amino Acid

<400> 214

```
Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln Leu Thr
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Asn Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu
            20                  25                  30
Tyr Val Asn Gly Phe Asn Pro Trp Ser Ser Val Pro Thr Thr Ser Thr
        35                  40                  45
Pro Gly Thr Ser Thr Val His Leu Ala Thr Ser Gly Thr Pro Ser Ser
    50                  55                  60
Leu Pro Gly His Thr Ala Pro Val Pro Leu Leu Ile Pro Phe Thr Leu
65                  70                  75                  80
Asn Phe Thr Ile Thr Asn Leu His Tyr Glu Glu Asn Met Gln His Pro
                85                  90                  95
Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu
            100                 105                 110
Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys
        115                 120                 125
Arg Leu Thr Leu Leu Arg Pro Glu Lys His Gly Ala Ala Thr Gly Val
```

```
    130                 135                 140
Asp Ala Ile Cys Thr Leu Arg Leu Asp Pro Thr Gly Pro Gly Leu Asp
145                 150                 155                 160
Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln Leu Thr Asn Ser Val Thr
                165                 170                 175
Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly
            180                 185                 190
Phe Thr His Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Ser
        195                 200                 205
Ala Val His Leu Glu Thr Ser Gly Thr Pro Ala Ser Leu Pro Gly His
    210                 215                 220
Thr Ala Pro Gly Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile
225                 230                 235                 240
Thr Asn Leu Gln Tyr Glu Glu Asp Met Arg His Pro Gly Ser Arg Lys
                245                 250                 255
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Lys Pro Leu Phe
            260                 265                 270
Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu
        275                 280                 285
Leu Arg Pro Glu Lys Arg Gly Ala Ala Thr Gly Val Asp Thr Ile Cys
    290                 295                 300
Thr His Arg Leu Asp Pro Leu Asn Pro Gly Leu Asp Arg Glu Gln Leu
305                 310                 315                 320
Tyr Trp Glu Leu Ser Lys Leu Thr Arg Gly Ile Ile Glu Leu Gly Pro
                325                 330                 335
Tyr Leu Leu Asp Arg Gly Ser Leu Tyr Val Asn Gly Phe Thr His Arg
            340                 345                 350
Asn Phe Val Pro Ile Thr Ser Thr Pro Gly Thr Ser Thr Val His Leu
        355                 360                 365
Gly Thr Ser Glu Thr Pro Ser Ser Leu Pro Arg Pro Ile Val Pro Gly
    370                 375                 380
Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln
385                 390                 395                 400
Tyr Glu Glu Ala Met Arg His Pro Gly Ser Arg Lys Phe Asn Thr Thr
                405                 410                 415
Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Leu Phe Lys Asn Thr Ser
            420                 425                 430
Ile Gly Pro Leu Tyr Ser Ser Cys Arg Leu Thr Leu Leu Arg Pro Glu
        435                 440                 445
Lys Asp Lys Ala Ala Thr Arg Val Asp Ala Ile Cys Thr His His Pro
    450                 455                 460
Asp Pro Gln Ser Pro Gly Leu Asn Arg Glu Gln Leu Tyr Trp Glu Leu
465                 470                 475                 480
Ser Gln Leu Thr His Gly Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp
                485                 490                 495
Arg Asp Ser Leu Tyr Val Asp Gly Phe Thr His Trp Ser Pro Ile Pro
            500                 505                 510
Thr Thr Ser Thr Pro Gly Thr Ser Ile Val Asn Leu Gly Thr Ser Gly
        515                 520                 525
Ile Pro Pro Ser Leu Pro Glu Thr Thr Ala Thr Gly Pro Leu Leu Val
    530                 535                 540
Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Gln Tyr Glu Glu Asn
545                 550                 555                 560
Met Gly His Pro Gly Ser Arg Lys Phe Asn Ile Thr Glu Ser Val Leu
                565                 570                 575
Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser Thr Ser Val Gly Pro Leu
            580                 585                 590
Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Val
```

```
        595                 600                 605
Ala Thr Arg Val Asp Ala Ile Cys Thr His Arg Pro Asp Pro Lys Ile
    610                 615                 620
Pro Gly Leu Asp Arg Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr
625                 630                 635                 640
His Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu
                645                 650                 655
Tyr Val Asn Gly Phe Thr Gln Arg Ser Ser Val Pro Thr Thr Ser Thr
            660                 665                 670
Pro Gly Thr Phe Thr Val Gln Pro Glu Thr Ser Glu Thr Pro Ser Ser
        675                 680                 685
Leu Pro Gly Pro Thr Ala Thr Gly Pro Val Leu Leu Pro Phe Thr Leu
    690                 695                 700
Asn Phe Thr Ile Ile Asn Leu Gln Tyr Glu Glu Asp Met His Arg Pro
705                 710                 715                 720
Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu
                725                 730                 735
Met Pro Leu Phe Lys Asn Thr Ser Val Ser Ser Leu Tyr Ser Gly Cys
            740                 745                 750
Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Arg Val
        755                 760                 765
Asp Ala Val Cys Thr His Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp
    770                 775                 780
Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr His Gly Ile Thr
785                 790                 795                 800
Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu Tyr Val Asn Gly
                805                 810                 815
Phe Thr His Gln Ser Ser Met Thr Thr Thr Arg Thr Pro Asp Thr Ser
            820                 825                 830
Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser Leu Ser Gly Pro
        835                 840                 845
Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile Asn Phe Thr Ile
    850                 855                 860
Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro Gly Ser Arg Lys
865                 870                 875                 880
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Val Phe
                885                 890                 895
Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu
            900                 905                 910
Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val Asp Ala Ile Cys
        915                 920                 925
Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp Arg Glu Gln Leu
    930                 935                 940
Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro
945                 950                 955                 960
Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg
                965                 970                 975
Ser Ser Val Pro Thr Thr Ser Ile Pro Gly Thr Pro Thr Val Asp Leu
            980                 985                 990
Gly Thr Ser Gly Thr Pro Val Ser Lys Pro Gly Pro Ser Ala Ala Ser
        995                 1000                1005
Pro Leu Leu Val Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Arg
    1010                1015                1020
Tyr Glu Glu Asn Met Gln His Pro Gly Ser Arg Lys Phe Asn Thr Thr
1025                1030                1035                1040
Glu Arg Val Leu Gln Gly Leu Leu Arg Ser Leu Phe Lys Ser Thr Ser
                1045                1050                1055
Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu
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1060 1065 1070
Lys Asp Gly Thr Ala Thr Gly Val Asp Ala Ile Cys Thr His His Pro
1075 1080 1085
Asp Pro Lys Ser Pro Arg Leu Asp Arg Glu Gln Leu Tyr Trp Glu Leu
1090 1095 1100
Ser Gln Leu Thr His Asn Ile Thr Glu Leu Gly His Tyr Ala Leu Asp
1105 1110 1115 1120
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Val Val Ser Glu Glu Pro Phe Thr Leu Asn Phe Thr Ile Asn Asn Leu
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<213> Homo sapiens

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Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln Leu Thr His Gly Ile Thr
50 55 60
Glu Leu Gly Pro Tyr Thr Leu Asp Arg His Ser Leu Tyr Val Asn Gly
65 70 75 80
Phe Thr His Gln Ser Ser Met Thr Thr Thr Arg Thr Pro Asp Thr Ser
85 90 95
Thr Met His Leu Ala Thr Ser Arg Thr Pro Ala Ser Leu Ser Gly Pro
100 105 110
Thr Thr Ala Ser Pro Leu Leu Val Leu Phe Thr Ile Asn Phe Thr Ile
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Thr Asn Leu Arg Tyr Glu Glu Asn Met His His Pro Gly Ser Arg Lys
130 135 140
Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Val Phe
145 150 155 160
Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu
165 170 175
Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr Lys Val Asp Ala Ile Cys
180 185 190
Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly Leu Asp Arg Glu Gln Leu
195 200 205
Tyr Trp Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro
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Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg

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Gly Thr Ser Gly Thr Pro Val Ser Lys Pro Gly Pro Ser Ala Ala Ser
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Pro Leu Leu Val Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu Arg
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Tyr Glu Glu Asn Met Gln His Pro Gly Ser Arg Lys Phe Asn Thr Thr
    290                 295                 300
Glu Arg Val Leu Gln Gly Leu Leu Arg Ser Leu Phe Lys Ser Thr Ser
305                 310                 315                 320
Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu
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Lys Asp Gly Thr Ala Thr Gly Val Asp Ala Ile Cys Thr His His Pro
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Asp Pro Lys Ser Pro Arg Leu Asp Arg Glu Gln Leu Tyr Trp Glu Leu
        355                 360                 365
Ser Gln Leu Thr His Asn Ile Thr Glu Leu Gly His Tyr Ala Leu Asp
    370                 375                 380
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Gly Leu Asp Arg Glu Gln Leu Tyr Leu Glu Leu Ser Gln Leu Thr His
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Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr
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545                 550                 555                 560
Val Val Ser Glu Glu Pro Phe Thr Leu Asn Phe Thr Ile Asn Asn Leu
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Arg Tyr Met Ala Asp Met Gly Gln Pro Gly Ser Leu Lys Phe Asn Ile
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Thr Asp Asn Val Met Lys His Leu Leu Ser Pro Leu Phe Gln Arg Ser
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Ser Leu Gly Ala Arg Tyr Thr Gly Cys Arg Val Ile Ala Leu Arg Ser
    610                 615                 620
Val Lys Asn Gly Ala Glu Thr Arg Val Asp Leu Leu Cys Thr Tyr Leu
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Gln Pro Leu Ser Gly Pro Gly Leu Pro Ile Lys Gln Val Phe His Glu
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Leu Ser Gln Gln Thr His Gly Ile Thr Arg Leu Gly Pro Tyr Ser Leu
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Glu Pro Pro Thr Thr Pro Lys Pro Ala Thr Thr Phe Leu Pro Pro Leu
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Ser Ala Thr Phe Asn Ser Thr Glu Gly Val Leu Gln His Leu Leu Arg
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Pro Leu Phe Gln Lys Ser Ser Met Gly Pro Phe Tyr Leu Gly Cys Gln
        755                 760                 765
Leu Ile Ser Leu Arg Pro Glu Lys Asp Gly Ala Ala Thr Gly Val Asp
    770                 775                 780
Thr Thr Cys Thr Tyr His Pro Asp Pro Val Gly Pro Gly Leu Asp Ile
785                 790                 795                 800
Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Gly Val Thr Gln
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Leu Gly Phe Tyr Val Leu Asp Arg Asp Ser Leu Phe Ile Asn Gly Tyr
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Ala Pro Gln Asn Leu Ser Ile Arg Gly Glu Tyr Gln Ile Asn Phe His
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Ile Val Asn Trp Asn Leu Ser Asn Pro Asp Pro Thr Ser Ser Glu Tyr
    850                 855                 860
Ile Thr Leu Leu Arg Asp Ile Gln Asp Lys Val Thr Thr Leu Tyr Lys
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Gly Ser Gln Leu His Asp Thr Phe Arg Phe Cys Leu Val Thr Asn Leu
                885                 890                 895
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            900                 905                 910
Leu Asp Pro Ser Leu Val Glu Gln Val Phe Leu Asp Lys Thr Leu Asn
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Ala Ser Phe His Trp Leu Gly Ser Thr Tyr Gln Leu Val Asp Ile His
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Val Thr Glu Met Glu Ser Ser Val Tyr Gln Pro Thr Ser Ser Ser Ser
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Thr Gln His Phe Tyr Pro Asn Phe Thr Ile Thr Asn Leu Pro Tyr Ser
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Gln Asp Lys Ala Gln Pro Gly Thr Thr Asn Tyr Gln Arg Asn Lys Arg
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Asn Ile Glu Asp Ala Leu Asn Gln Leu Phe Arg Asn Ser Ser Ile Lys
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Leu Val Asp Gly Tyr Ser Pro Asn Arg Asn Glu Pro Leu Thr Gly Asn
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Ser Asp Leu Pro Phe Trp Ala Val Ile Phe Ile Gly Leu Ala Gly Leu
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50 55 60
Ser Gly Thr Pro Ser Ser Leu Pro Gly His Thr Ala Pro Val Pro Leu
65 70 75 80
Leu Ile Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn Leu His Tyr Glu
85 90 95
Glu Asn Met Gln His Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg
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115 120 125
Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys His
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Gly Ala Ala Thr Gly Val Asp Ala Ile Cys Thr Leu Arg Leu Asp Pro
145 150 155 160
Thr Gly Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Glu Leu Ser Gln
165 170 175
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180 185 190
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Ala Ser Leu Pro Gly His Thr Ala Pro Gly Pro Leu Leu Val Pro Phe
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260 265 270
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275 280 285
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290 295 300
Gly Val Asp Thr Ile Cys Thr His Arg Leu Asp Pro Leu Asn Pro Gly
305 310 315 320
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325 330 335
Ile Ile Glu Leu Gly Pro Tyr Leu Leu Asp Arg Gly Ser Leu Tyr Val
340 345 350
Asn Gly Phe Thr His Arg Asn Phe Val Pro Ile Thr Ser Thr Pro Gly
355 360 365
Thr Ser Thr Val His Leu Gly Thr Ser Glu Thr Pro Ser Ser Leu Pro
370 375 380
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385 390 395 400
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Ile Cys Thr His His Pro Asp Pro Gln Ser Pro Gly Leu Asn Arg Glu
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Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Gly Ile Thr Glu Leu
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Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val Asp Gly Phe Thr
            500                 505                 510
His Trp Ser Pro Ile Pro Thr Thr Ser Thr Pro Gly Thr Ser Ile Val
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Thr Gly Pro Leu Leu Val Pro Phe Thr Leu Asn Phe Thr Ile Thr Asn
545                 550                 555                 560
Leu Gln Tyr Glu Glu Asn Met Gly His Pro Gly Ser Arg Lys Phe Asn
                565                 570                 575
Ile Thr Glu Ser Val Leu Gln Gly Leu Leu Lys Pro Leu Phe Lys Ser
            580                 585                 590
Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg
        595                 600                 605
Pro Glu Lys Asp Gly Val Ala Thr Arg Val Asp Ala Ile Cys Thr His
    610                 615                 620
Arg Pro Asp Pro Lys Ile Pro Gly Leu Asp Arg Gln Gln Leu Tyr Trp
625                 630                 635                 640
Glu Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro Tyr Thr
                645                 650                 655
Leu Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr Gln Arg Ser Ser
            660                 665                 670
Val Pro Thr Thr Ser Thr Pro Gly Thr Phe Thr Val Gln Pro Glu Thr
        675                 680                 685
Ser Glu Thr Pro Ser Ser Leu Pro Gly Pro Thr Ala Thr Gly Pro Val
    690                 695                 700
Leu Leu Pro Phe Thr Leu Asn Phe Thr Ile Ile Asn Leu Gln Tyr Glu
705                 710                 715                 720
Glu Asp Met His Arg Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg
                725                 730                 735
Val Leu Gln Gly Leu Leu Met Pro Leu Phe Lys Asn Thr Ser Val Ser
            740                 745                 750
Ser Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro Glu Lys Asp
        755                 760                 765
Gly Ala Ala Thr Arg Val Asp Ala Val Cys Thr His Arg Pro Asp Pro
    770                 775                 780
Lys Ser Pro Gly Leu Asp Arg Glu Arg Leu Tyr Trp Lys Leu Ser Gln
785                 790                 795                 800
Leu Thr His Gly Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg His
                805                 810                 815
Ser Leu Tyr Val Asn Gly Phe Thr His Gln Ser Ser Met Thr Thr Thr
            820                 825                 830
Arg Thr Pro Asp Thr Ser Thr Met His Leu Ala Thr Ser Arg Thr Pro
        835                 840                 845
Ala Ser Leu Ser Gly Pro Thr Thr Ala Ser Pro Leu Leu Val Leu Phe
    850                 855                 860
Thr Ile Asn Phe Thr Ile Thr Asn Leu Arg Tyr Glu Glu Asn Met His
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His Pro Gly Ser Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly
                885                 890                 895
Leu Leu Arg Pro Val Phe Lys Asn Thr Ser Val Gly Pro Leu Tyr Ser
            900                 905                 910
Gly Cys Arg Leu Thr Leu Leu Arg Pro Lys Lys Asp Gly Ala Ala Thr
        915                 920                 925
Lys Val Asp Ala Ile Cys Thr Tyr Arg Pro Asp Pro Lys Ser Pro Gly
    930                 935                 940
Leu Asp Arg Glu Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Ser
945                 950                 955                 960
Ile Thr Glu Leu Gly Pro Tyr Thr Leu Asp Arg Asp Ser Leu Tyr Val
                965                 970                 975
Asn Gly Phe Thr Gln Arg Ser Ser Val Pro Thr Thr Ser Ile Pro Gly
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Thr Pro Thr Val Asp Leu Gly Thr Ser Gly Thr Pro Val Ser Lys Pro
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Gly Pro Ser Ala Ala Ser Pro Leu Leu Val Leu Phe Thr Leu Asn Phe
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Thr Ile Thr Asn Leu Arg Tyr Glu Glu Asn Met Gln His Pro Gly Ser
1025                1030                1035                1040
Arg Lys Phe Asn Thr Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Ser
                1045                1050                1055
Leu Phe Lys Ser Thr Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu
            1060                1065                1070
Thr Leu Leu Arg Pro Glu Lys Asp Gly Thr Ala Thr Gly Val Asp Ala
        1075                1080                1085
Ile Cys Thr His His Pro Asp Pro Lys Ser Pro Arg Leu Asp Arg Glu
    1090                1095                1100
Gln Leu Tyr Trp Glu Leu Ser Gln Leu Thr His Asn Ile Thr Glu Leu
1105                1110                1115                1120
Gly Pro Tyr Ala Leu Asp Asn Asp Ser Leu Phe Val Asn Gly Phe Thr
                1125                1130                1135
His Arg Ser Ser Val Ser Thr Thr Ser Thr Pro Gly Thr Pro Thr Val
            1140                1145                1150
Tyr Leu Gly Ala Ser Lys Thr Pro Ala Ser Ile Phe Gly Pro Ser Ala
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Ala Ser His Leu Leu Ile Leu Phe Thr Leu Asn Phe Thr Ile Thr Asn
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Leu Arg Tyr Glu Glu Asn Met Trp Pro Gly Ser Arg Lys Phe Asn Thr
1185                1190                1195                1200
Thr Glu Arg Val Leu Gln Gly Leu Leu Arg Pro Leu Phe Lys Asn Thr
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Ser Val Gly Pro Leu Tyr Ser Gly Cys Arg Leu Thr Leu Leu Arg Pro
            1220                1225                1230
Glu Lys Asp Gly Glu Ala Thr Gly Val Asp Ala Ile Cys Thr His Arg
        1235                1240                1245
Pro Asp Pro Thr Gly Pro Gly Leu Asp Arg Glu Gln Leu Tyr Leu Glu
    1250                1255                1260
Leu Ser Gln Leu Thr His Ser Ile Thr Glu Leu Gly Pro Tyr Thr Leu
1265                1270                1275                1280
Asp Arg Asp Ser Leu Tyr Val Asn Gly Phe Thr His Arg Ser Ser Val
                1285                1290                1295
Pro Thr Thr Ser Thr Gly Val Val Ser Glu Glu Pro Phe Thr Leu Asn
            1300                1305                1310
Phe Thr Ile Asn Asn Leu Arg Tyr Met Ala Asp Met Gly Gln Pro Gly
        1315                1320                1325
Ser Leu Lys Phe Asn Ile Thr Asp Asn Val Met Gln His Leu Leu Ser
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Pro Leu Phe Gln Arg Ser Ser Leu Gly Ala Arg Tyr Thr Gly Cys Arg
1345                1350                1355                1360
Val Ile Ala Leu Arg Ser Val Lys Asn Gly Ala Glu Thr Arg Val Asp
                1365                1370                1375
Leu Leu Cys Thr Tyr Leu Gln Pro Leu Ser Gly Pro Gly Leu Pro Ile
            1380                1385                1390
Lys Gln Val Phe His Glu Leu Ser Gln Gln Thr His Gly Ile Thr Arg
        1395                1400                1405
Leu Gly Pro Tyr Ser Leu Asp Lys Asp Ser Leu Tyr Leu Asn Gly Tyr
    1410                1415                1420
Asn Glu Pro Gly Pro Asp Glu Pro Pro Thr Thr Pro Lys Pro Ala Thr
1425                1430                1435                1440
Thr Phe Leu Pro Pro Leu Ser Glu Ala Thr Thr Ala Met Gly Tyr His
                1445                1450                1455
Leu Lys Thr Leu Thr Leu Asn Phe Thr Ile Ser Asn Leu Gln Tyr Ser
            1460                1465                1470
Pro Asp Met Gly Lys Gly Ser Ala Thr Phe Asn Ser Thr Glu Gly Val
        1475                1480                1485
Leu Gln His Leu Leu Arg Pro Leu Phe Gln Lys Ser Ser Met Gly Pro
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Phe Tyr Leu Gly Cys Gln Leu Ile Ser Leu Arg Pro Glu Lys Asp Gly
1505                1510                1515                1520
Ala Ala Thr Gly Val Asp Thr Thr Cys Thr Tyr His Pro Asp Pro Val
                1525                1530                1535
Gly Pro Gly Leu Asp Ile Gln Gln Leu Tyr Trp Glu Leu Ser Gln Leu
            1540                1545                1550
Thr His Gly Val Thr Gln Leu Gly Phe Tyr Val Leu Asp Arg Asp Ser
        1555                1560                1565
Leu Phe Ile Asn Gly Tyr Ala Pro Gln Asn Leu Ser Ile Arg Gly Glu
    1570                1575                1580
Tyr Gln Ile Asn Phe His Ile Val Asn Trp Asn Leu Ser Asn Pro Asp
1585                1590                1595                1600
Pro Thr Ser Ser Glu Tyr Ile Thr Leu Leu Arg Asp Ile Gln Asp Lys
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Val Thr Thr Leu Tyr Lys Gly Ser Gln Leu His Asp Thr Phe Arg Phe
            1620                1625                1630
Cys Leu Val Thr Asn Leu Thr Met Asp Ser Val Leu Val Thr Val Lys
        1635                1640                1645
Ala Leu Phe Ser Ser Asn Leu Asp Pro Ser Leu Val Glu Gln Val Phe
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Leu Asp Lys Thr Leu Asn Ala Ser Phe His Trp Leu Gly Ser Thr Tyr
1665                1670                1675                1680
Gln Leu Val Asp Ile His Val Thr Glu Met Glu Ser Ser Val Tyr Gln
                1685                1690                1695
Pro Thr Ser Ser Ser Ser Thr Gln His Phe Tyr Pro Asn Phe Thr Ile
            1700                1705                1710
Thr Asn Leu Pro Tyr Ser Gln Asp Lys Ala Gln Pro Gly Thr Thr Asn
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Tyr Gln Arg Asn Lys Arg Asn Ile Glu Asp Ala Leu Asn Gln Leu Phe
    1730                1735                1740
Arg Asn Ser Ser Ile Lys Ser Tyr Phe Ser Asp Cys Gln Val Ser Thr
1745                1750                1755                1760
Phe Arg Ser Val Pro Asn Arg His His Thr Gly Val Asp Ser Leu Cys
                1765                1770                1775
Asn Phe Ser Pro Leu Ala Arg Arg Val Asp Arg Val Ala Ile Tyr Glu
            1780                1785                1790
Glu Phe Leu Arg Met Thr Arg Asn Gly Thr Gln Leu Gln Asn Phe Thr
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        1795                1800                1805
Leu Asp Arg Ser Ser Val Leu Val Asp Gly Tyr Ser Pro Asn Arg Asn
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Glu Pro Leu Thr Gly Asn Ser Asp Leu Pro Phe Trp Ala Val Ile Leu
1825                1830                1835                1840
Ile Gly Leu Ala Gly Leu Leu Gly Leu Ile Thr Cys Leu Ile Cys Gly
                1845                1850                1855
Val Leu Val Thr Thr Arg Arg Arg Lys Lys Glu Gly Glu Tyr Asn Val
            1860                1865                1870
Gln Gln Gln Cys Pro Gly Tyr Tyr Gln Ser His Leu Asp Leu Glu Asp
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Leu Gln
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<212> DNA
<213> Homo sapiens

<400> 218

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<211> 1465
<212> PRT
<213> Homo sapiens

<400> 219

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Ala Ser Lys Lys Arg Ala Ser Thr Gln Ala Ser Ser Gln Lys Ser Leu

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Ser Gln Arg Ser Ser Ser Gln Arg Ala Ser Ser Gln Thr Ser Leu Gly
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Gly Thr Ile Cys Arg Val Cys Ala Lys Arg Val Ser Thr Gln Glu Asp
65                  70                  75                  80
Glu Glu Gln Glu Asn Arg Ser Arg Tyr Gln Ser Leu Val Ala Ala Tyr
                85                  90                  95
Gly Glu Ala Lys Arg His Gly Phe Leu Ser Glu Leu Ala His Leu Glu
            100                 105                 110
Glu Asp Val His Leu Ala Arg Ser Gln Ala Arg Asp Lys Leu Asp Lys
        115                 120                 125
Tyr Ala Ile Gln Gln Met Met Glu Asp Lys Leu Ala Trp Glu Arg His
    130                 135                 140
Thr Phe Glu Glu Arg Ile Ser Arg Ala Pro Glu Ile Leu Val Arg Leu
145                 150                 155                 160
Arg Ser His Thr Val Trp Glu Arg Met Ser Val Lys Leu Cys Phe Thr
                165                 170                 175
Val Gln Gly Phe Pro Thr Pro Val Val Gln Trp Tyr Lys Asp Gly Ser
            180                 185                 190
Leu Ile Cys Gln Ala Ala Glu Pro Gly Lys Tyr Arg Ile Glu Ser Asn
        195                 200                 205
Tyr Gly Val His Thr Leu Glu Ile Asn Arg Ala Asp Phe Asp Asp Thr
    210                 215                 220
Ala Thr Tyr Ser Ala Val Ala Thr Asn Ala His Gly Gln Val Ser Thr
225                 230                 235                 240
Asn Ala Ala Val Val Val Arg Arg Phe Arg Gly Asp Glu Glu Pro Phe
                245                 250                 255
Arg Ser Val Gly Leu Pro Ile Gly Leu Pro Leu Ser Ser Met Ile Pro
            260                 265                 270
Tyr Thr His Phe Asp Val Gln Phe Leu Glu Lys Phe Gly Val Thr Phe
        275                 280                 285
Arg Arg Glu Gly Glu Thr Val Thr Leu Lys Cys Thr Met Leu Val Thr
    290                 295                 300
Pro Asp Leu Lys Arg Val Gln Pro Arg Ala Glu Trp Tyr Arg Asp Asp
305                 310                 315                 320
Leu Leu Leu Lys Glu Ser Lys Trp Thr Lys Met Phe Phe Gly Glu Gly
                325                 330                 335
Gln Ala Ser Leu Ser Phe Ser His Leu His Lys Asp Asp Glu Gly Leu
            340                 345                 350
Tyr Thr Leu Arg Ile Val Ser Arg Gly Gly Val Thr Asp His Ser Ala
        355                 360                 365
Phe Leu Phe Val Arg Asp Ala Asp Pro Leu Val Thr Gly Ala Pro Gly
    370                 375                 380
Ala Pro Met Asp Leu Gln Cys His Asp Ala Asn Arg Asp Tyr Val Ile
385                 390                 395                 400
Val Thr Trp Lys Pro Pro Asn Thr Thr Thr Glu Ser Pro Val Met Gly
                405                 410                 415
Tyr Phe Val Asp Arg Cys Glu Val Gly Thr Asn Asn Trp Val Gln Cys
            420                 425                 430
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Glu Gly Arg Ser Tyr Ile Phe Arg Val Arg Ala Val Asn Ser Ala Gly
    450                 455                 460
Ile Ser Arg Pro Ser Arg Val Ser Asp Ala Val Ala Ala Leu Asp Pro
465                 470                 475                 480
Leu Asp Leu Arg Arg Leu Gln Ala Val His Leu Glu Gly Glu Lys Glu
                485                 490                 495
Ile Ala Ile Tyr Gln Asp Asp Leu Glu Gly Asp Ala Gln Val Pro Gly
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Leu Ser Trp Glu Pro Pro Thr Pro Arg Gly Lys Asp Pro Leu Met Tyr
    530                 535                 540
Phe Ile Glu Lys Ser Val Val Gly Ser Gly Thr Trp Gln Arg Val Asn
545                 550                 555                 560
Ala Gln Thr Ala Val Arg Ser Pro Arg Tyr Ala Val Phe Asp Leu Met
                565                 570                 575
Glu Gly Lys Ser Tyr Val Phe Arg Val Leu Ser Ala Asn Arg His Gly
            580                 585                 590
Leu Ser Glu Pro Ser Glu Ile Thr Ser Pro Ile Gln Ala Gln Asp Val
        595                 600                 605
Thr Val Val Pro Ser Ala Pro Gly Arg Val Leu Ala Ser Arg Asn Thr
    610                 615                 620
Lys Thr Ser Val Val Val Gln Trp Asp Arg Pro Lys His Glu Glu Asp
625                 630                 635                 640
Leu Leu Gly Tyr Tyr Val Asp Cys Cys Val Ala Gly Thr Asn Leu Trp
                645                 650                 655
Glu Pro Cys Asn His Lys Pro Ile Gly Tyr Asn Arg Phe Val Val His
            660                 665                 670
Gly Leu Thr Thr Gly Glu Gln Tyr Ile Phe Arg Val Lys Ala Val Asn
        675                 680                 685
Ala Val Gly Met Ser Glu Asn Ser Gln Glu Ser Asp Val Ile Lys Val
    690                 695                 700
Gln Ala Ala Leu Thr Val Pro Ser His Pro Tyr Gly Ile Thr Leu Leu
705                 710                 715                 720
Asn Cys Asp Gly His Ser Met Thr Leu Gly Trp Lys Val Pro Lys Phe
                725                 730                 735
Ser Gly Gly Ser Pro Ile Leu Gly Tyr Tyr Leu Asp Lys Arg Glu Val
            740                 745                 750
His His Lys Asn Trp His Glu Val Asn Ser Ser Pro Ser Lys Pro Thr
        755                 760                 765
Ile Leu Thr Val Asp Gly Leu Thr Glu Gly Ser Leu Tyr Glu Phe Lys
    770                 775                 780
Ile Ala Ala Val Asn Leu Ala Gly Ile Gly Glu Pro Ser Asp Pro Ser
785                 790                 795                 800
Glu His Phe Lys Cys Glu Ala Trp Thr Met Pro Glu Pro Gly Pro Ala
                805                 810                 815
Tyr Asp Leu Thr Phe Cys Glu Val Arg Asp Thr Ser Leu Val Met Leu
            820                 825                 830
Trp Lys Ala Pro Val Tyr Ser Gly Ser Ser Pro Val Ser Gly Tyr Phe
        835                 840                 845
Val Asp Phe Arg Glu Glu Asp Ala Gly Glu Trp Ile Thr Val Asp Gln
    850                 855                 860
Thr Thr Thr Ala Ser Arg Tyr Leu Lys Val Ser Asp Leu Gln Gln Gly
865                 870                 875                 880
Lys Thr Tyr Val Phe Arg Val Arg Ala Val Asn Ala Asn Gly Val Gly
                885                 890                 895
Lys Pro Ser Asp Thr Ser Glu Pro Val Leu Val Glu Ala Arg Pro Gly
            900                 905                 910
Thr Lys Glu Ile Ser Ala Gly Val Asp Glu Gln Gly Asn Ile Tyr Leu
        915                 920                 925
Gly Phe Asp Cys Gln Glu Met Thr Asp Ala Ser Gln Phe Thr Trp Cys
    930                 935                 940
Lys Ser Tyr Glu Glu Ile Ser Asp Asp Glu Arg Phe Lys Ile Glu Thr
945                 950                 955                 960
Val Gly Asp His Ser Lys Leu Tyr Leu Lys Asn Pro Asp Lys Glu Asp
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Asn Glu Ile Lys Asn Pro Thr Ile Pro Leu Lys Ser Glu Leu Ala Tyr
    1010                1015                1020
Glu Ile Phe Asp Lys Gly Arg Val Arg Phe Trp Leu Gln Ala Glu His
1025                1030                1035                1040
Leu Ser Pro Asp Ala Ser Tyr Arg Phe Ile Ile Asn Asp Arg Glu Val
                1045                1050                1055
Ser Asp Ser Glu Ile His Arg Ile Lys Cys Asp Lys Ala Thr Gly Ile
            1060                1065                1070
Ile Glu Met Val Met Asp Arg Phe Ser Ile Glu Asn Glu Gly Thr Tyr
        1075                1080                1085
Thr Val Gln Ile His Asp Gly Lys Ala Lys Ser Gln Ser Ser Leu Val
    1090                1095                1100
Leu Ile Gly Asp Ala Phe Lys Thr Val Leu Glu Glu Ala Glu Phe Gln
1105                1110                1115                1120
Arg Lys Glu Phe Leu Arg Lys Gln Gly Pro His Phe Ala Glu Tyr Leu
                1125                1130                1135
His Trp Asp Val Thr Glu Glu Cys Glu Val Arg Leu Val Cys Lys Val
            1140                1145                1150
Ala Asn Thr Lys Lys Glu Thr Val Phe Lys Trp Leu Lys Asp Asp Ala
        1155                1160                1165
Leu Tyr Glu Thr Glu Thr Leu Pro Asn Leu Glu Arg Gly Ile Cys Glu
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Leu Leu Ile Pro Lys Leu Ser Lys Lys Asp His Gly Glu Tyr Lys Ala
1185                1190                1195                1200
Thr Leu Lys Asp Asp Arg Gly Gln Asp Val Ser Ile Leu Glu Ile Ala
                1205                1210                1215
Gly Lys Val Tyr Asp Asp Met Ile Leu Ala Met Ser Arg Val Cys Gly
            1220                1225                1230
Lys Ser Ala Ser Pro Leu Lys Val Leu Cys Thr Pro Glu Gly Ile Arg
        1235                1240                1245
Leu Gln Cys Phe Met Lys Tyr Phe Thr Asp Glu Met Lys Val Asn Trp
    1250                1255                1260
Cys His Lys Asp Ala Lys Ile Ser Ser Ser Glu His Met Arg Ile Gly
1265                1270                1275                1280
Gly Ser Glu Glu Met Ala Trp Leu Gln Ile Cys Glu Pro Thr Glu Lys
                1285                1290                1295
Asp Lys Gly Lys Tyr Thr Phe Glu Ile Phe Asp Gly Lys Asp Asn His
            1300                1305                1310
Gln Arg Ser Leu Asp Leu Ser Gly Gln Ala Phe Asp Glu Ala Phe Ala
        1315                1320                1325
Glu Phe Gln Gln Phe Lys Ala Ala Ala Phe Ala Glu Lys Asn Arg Gly
    1330                1335                1340
Arg Leu Ile Gly Gly Leu Pro Asp Val Val Thr Ile Met Glu Gly Lys
1345                1350                1355                1360
Thr Leu Asn Leu Thr Cys Thr Val Phe Gly Asn Pro Asp Pro Glu Val
                1365                1370                1375
Ile Trp Phe Lys Asn Asp Gln Asp Ile Gln Leu Ser Glu His Phe Ser
            1380                1385                1390
Val Lys Val Glu Gln Ala Lys Tyr Val Ser Met Thr Ile Lys Gly Val
        1395                1400                1405
Thr Ser Glu Asp Ser Gly Lys Tyr Ser Ile Asn Ile Lys Asn Lys Tyr
    1410                1415                1420
Gly Gly Glu Lys Ile Asp Val Thr Val Ser Val Tyr Lys His Gly Glu
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1425 1430 1435 1440
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1460 1465

<210> 220
<211> 4135
<212> DNA
<213> Homo sapiens

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<210> 221
<211> 689
<212> PRT
<213> Homo sapiens

<400> 221

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            20                  25                  30
Lys Glu Thr Asn Lys Asn Asn Thr Glu Ala Pro Val Thr Lys Ile Glu
        35                  40                  45
Leu Leu Pro Ser Tyr Ser Thr Ala Thr Leu Ile Asp Glu Pro Thr Glu
    50                  55                  60
Val Asp Asp Pro Trp Asn Leu Pro Thr Leu Gln Asp Ser Gly Ile Lys
65                  70                  75                  80
Trp Ser Glu Arg Asp Thr Lys Gly Lys Ile Leu Cys Phe Phe Gln Gly
                85                  90                  95
Ile Gly Arg Leu Ile Leu Leu Leu Gly Phe Leu Tyr Phe Phe Val Cys
            100                 105                 110
Ser Leu Asp Ile Leu Ser Ser Ala Phe Gln Leu Val Gly Gly Lys Met
        115                 120                 125
Ala Gly Gln Phe Phe Ser Asn Ser Ser Ile Met Ser Asn Pro Leu Leu
    130                 135                 140
Gly Leu Val Ile Gly Val Leu Val Thr Val Leu Val Gln Ser Ser Ser
145                 150                 155                 160
Thr Ser Thr Ser Ile Val Val Ser Met Val Ser Ser Ser Leu Leu Thr
                165                 170                 175
Val Arg Ala Ala Ile Pro Ile Ile Met Gly Ala Asn Ile Gly Thr Ser
            180                 185                 190
Ile Thr Asn Thr Ile Val Ala Leu Met Gln Val Gly Asp Arg Ser Glu
        195                 200                 205
Phe Arg Arg Ala Phe Ala Gly Ala Thr Val His Asp Phe Phe Asn Trp
```

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    210                 215                 220
Leu Ser Leu Leu Val Leu Leu Pro Val Glu Val Ala Thr His Tyr Leu
225                 230                 235                 240
Glu Ile Ile Thr Gln Leu Ile Val Glu Ser Phe His Phe Lys Asn Gly
                245                 250                 255
Glu Asp Ala Pro Asp Leu Leu Lys Val Ile Thr Lys Pro Phe Thr Lys
            260                 265                 270
Leu Ile Val Gln Leu Asp Lys Lys Val Ile Ser Gln Ile Ala Met Asn
        275                 280                 285
Asp Glu Lys Ala Lys Asn Lys Ser Leu Val Lys Ile Trp Cys Lys Thr
    290                 295                 300
Phe Thr Asn Lys Thr Gln Ile Asn Val Thr Val Pro Ser Thr Ala Asn
305                 310                 315                 320
Cys Thr Ser Pro Ser Leu Cys Trp Thr Asp Gly Ile Gln Asn Trp Thr
                325                 330                 335
Met Lys Asn Val Thr Tyr Lys Glu Asn Ile Ala Lys Cys Gln His Ile
            340                 345                 350
Phe Val Asn Phe His Leu Pro Asp Leu Ala Val Gly Thr Ile Leu Leu
        355                 360                 365
Ile Leu Ser Leu Leu Val Leu Cys Gly Cys Leu Ile Met Ile Val Lys
    370                 375                 380
Ile Leu Gly Ser Val Leu Lys Gly Gln Val Ala Thr Val Ile Lys Lys
385                 390                 395                 400
Thr Ile Asn Thr Asp Phe Pro Phe Pro Phe Ala Trp Leu Thr Gly Tyr
                405                 410                 415
Leu Ala Ile Leu Val Gly Ala Gly Met Thr Phe Ile Val Gln Ser Ser
            420                 425                 430
Ser Val Phe Thr Ser Ala Leu Thr Pro Leu Ile Gly Ile Gly Val Ile
        435                 440                 445
Thr Ile Glu Arg Ala Tyr Pro Leu Thr Leu Gly Ser Asn Ile Gly Thr
    450                 455                 460
Thr Thr Thr Ala Ile Leu Ala Ala Leu Ala Ser Pro Gly Asn Ala Leu
465                 470                 475                 480
Arg Ser Ser Leu Gln Ile Ala Leu Cys His Phe Phe Phe Asn Ile Ser
                485                 490                 495
Gly Ile Leu Leu Trp Tyr Pro Ile Pro Phe Thr Arg Leu Pro Ile Arg
            500                 505                 510
Met Ala Lys Gly Leu Gly Asn Ile Ser Ala Lys Tyr Arg Trp Phe Ala
        515                 520                 525
Val Phe Tyr Leu Ile Ile Phe Phe Phe Leu Ile Pro Leu Thr Val Phe
    530                 535                 540
Gly Leu Ser Leu Ala Gly Trp Arg Val Leu Val Gly Val Gly Val Pro
545                 550                 555                 560
Val Val Phe Ile Ile Ile Leu Val Leu Cys Leu Arg Leu Leu Gln Ser
                565                 570                 575
Arg Cys Pro Arg Val Leu Pro Lys Lys Leu Gln Asn Trp Asn Phe Leu
            580                 585                 590
Pro Leu Trp Met Arg Ser Leu Lys Pro Trp Asp Ala Val Val Ser Lys
        595                 600                 605
Phe Thr Gly Cys Phe Gln Met Arg Cys Cys Cys Cys Cys Arg Val Cys
    610                 615                 620
Cys Arg Ala Cys Cys Leu Leu Cys Gly Cys Pro Lys Cys Cys Arg Cys
625                 630                 635                 640
Ser Lys Cys Cys Glu Asp Leu Glu Glu Ala Gln Glu Gly Gln Asp Val
                645                 650                 655
Pro Val Lys Ala Pro Glu Thr Phe Asp Asn Ile Thr Ile Ser Arg Glu
            660                 665                 670
Ala Gln Gly Glu Val Pro Ala Ser Asp Ser Lys Thr Glu Cys Thr Ala
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        675                 680                 685
Leu



<210> 222
<211> 771
<212> DNA
<213> Homo sapiens

<400> 222
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gatccggatt caccattgtt cagagaagaa aactacgcct cagccctgag caatgtagta 180
acttttatgt ggaaaagtat ggaaaaatgt tttccccaa cttaacagct tacatgagtt 240
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atcctaacaa acccaaactt tgtcaccatc caattgtaga agaaccttat taaaaaaaaa 660
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<210> 223
<211> 212
<212> PRT
<213> Homo sapiens

<400> 223
Met Glu Ile Ser Met Pro Pro Pro Gln Ile Tyr Val Glu Lys Thr Leu
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Ala Ile Ile Lys Pro Asp Ile Val Asp Lys Glu Glu Glu Ile Gln Asp
            20                  25                  30
Ile Ile Leu Arg Ser Gly Phe Thr Ile Val Gln Arg Arg Lys Leu Arg
        35                  40                  45
Leu Ser Pro Glu Gln Cys Ser Asn Phe Tyr Val Glu Lys Tyr Gly Lys
    50                  55                  60
Met Phe Phe Pro Asn Leu Thr Ala Tyr Met Ser Ser Gly Pro Leu Val
65                  70                  75                  80
Ala Met Ile Leu Ala Arg His Lys Ala Ile Ser Tyr Trp Leu Glu Leu
                85                  90                  95
Leu Gly Pro Asn Asn Ser Leu Val Ala Lys Glu Thr His Pro Asp Ser
            100                 105                 110
Leu Arg Ala Ile Tyr Gly Thr Asp Asp Leu Arg Asn Ala Leu His Gly
        115                 120                 125
Ser Asn Asp Phe Ala Ala Ala Glu Arg Glu Ile Arg Phe Met Phe Pro
    130                 135                 140
Glu Val Ile Val Glu Pro Ile Pro Ile Gly Gln Ala Ala Lys Asp Tyr
145                 150                 155                 160
Leu Asn Leu His Ile Met Pro Thr Leu Leu Glu Gly Leu Thr Glu Leu
                165                 170                 175
Cys Lys Gln Lys Pro Ala Asp Pro Leu Ile Trp Leu Ala Asp Trp Leu
            180                 185                 190
Leu Lys Asn Asn Pro Asn Lys Pro Lys Leu Cys His His Pro Ile Val
        195                 200                 205
Glu Glu Pro Tyr
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210

<210> 224
<211> 3463
<212> DNA
<213> Homo sapiens

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<210> 225
<211> 495
<212> PRT
<213> Homo sapiens

<400> 225
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20 25 30
Pro Arg Asp Arg Trp Met Phe Trp Ala Met Leu Pro Pro Pro Pro Pro
35 40 45
Pro Leu Thr Ser Ser Leu Pro Ala Ala Gly Ser Lys Pro Ser Ser Glu
50 55 60
Ser Gln Pro Pro Met Glu Ala Gln Ser Leu Pro Gly Ala Pro Pro Pro
65 70 75 80
Phe Asp Ala Gln Ile Leu Pro Gly Ala Gln Pro Pro Phe Asp Ala Gln
85 90 95
Ser Pro Leu Asp Ser Gln Pro Gln Pro Ser Gly Gln Pro Trp Asn Phe
100 105 110
His Ala Ser Thr Ser Trp Tyr Trp Arg Gln Ser Ser Asp Arg Phe Pro
115 120 125
Arg His Gln Lys Ser Phe Asn Pro Ala Val Lys Asn Ser Tyr Tyr Pro
130 135 140
Arg Lys Tyr Asp Ala Lys Phe Thr Asp Phe Ser Leu Pro Pro Ser Arg
145 150 155 160
Lys Gln Lys Lys Lys Lys Arg Lys Glu Pro Val Phe His Phe Phe Cys
165 170 175
Asp Thr Cys Asp Arg Gly Phe Lys Asn Gln Glu Lys Tyr Asp Lys His
180 185 190
Met Ser Glu His Thr Lys Cys Pro Glu Leu Asp Cys Ser Phe Thr Ala
195 200 205
His Glu Lys Ile Val Gln Phe His Trp Arg Asn Met His Ala Pro Gly
210 215 220
Met Lys Lys Ile Lys Leu Asp Thr Pro Glu Glu Ile Ala Arg Trp Arg
225 230 235 240
Glu Glu Arg Arg Lys Asn Tyr Pro Thr Leu Ala Asn Ile Glu Arg Lys
245 250 255
Lys Lys Leu Lys Leu Glu Lys Glu Lys Arg Gly Ala Val Leu Thr Thr
260 265 270
Thr Gln Tyr Gly Lys Met Lys Gly Met Ser Arg His Ser Gln Met Ala
275 280 285
Lys Ile Arg Ser Pro Gly Lys Asn His Lys Trp Lys Asn Asp Asn Ser
290 295 300
Arg Gln Arg Ala Val Thr Gly Ser Gly Ser His Leu Cys Asp Leu Lys
305 310 315 320
Leu Glu Gly Pro Pro Glu Ala Asn Ala Asp Pro Leu Gly Val Leu Ile
325 330 335

Asn Ser Asp Ser Glu Ser Asp Lys Glu Glu Lys Pro Gln His Ser Val
340 345 350
Ile Pro Lys Glu Val Thr Pro Ala Leu Cys Ser Leu Met Ser Ser Tyr
355 360 365
Gly Ser Leu Ser Gly Ser Glu Ser Glu Pro Glu Glu Thr Pro Ile Lys
370 375 380
Thr Glu Ala Asp Val Leu Ala Glu Asn Gln Val Leu Asp Ser Ser Ala
385 390 395 400
Pro Lys Ser Pro Ser Gln Asp Val Lys Ala Thr Val Arg Asn Phe Ser
405 410 415
Glu Ala Lys Ser Glu Asn Arg Lys Lys Ser Phe Glu Lys Thr Asn Pro
420 425 430
Lys Arg Lys Lys Asp Tyr His Asn Tyr Gln Thr Leu Phe Glu Pro Arg
435 440 445
Thr His His Pro Tyr Leu Leu Glu Met Leu Leu Ala Pro Asp Ile Arg
450 455 460
His Glu Arg Asn Val Ile Leu Gln Cys Val Arg Tyr Ile Ile Lys Lys
465 470 475 480
Asp Phe Phe Gly Leu Asp Thr Asn Ser Ala Lys Ser Lys Asp Val
485 490 495

<210> 226
<211> 942
<212> DNA
<213> Homo sapiens

<400> 226
atgagaattg cagtgatttg cttttgcctc ctaggcatca cctgtgccat accagttaaa 60
caggctgatt ctggaagttc tgaggaaaag cagctttaca acaaataccc agatgctgtg 120
gccacatggc taaaccctga cccatctcag aagcagaatc tcctagcccc acagaatgct 180
gtgtcctctg aagaaaccaa tgactttaaa caagagaccc ttccaagtaa gtccaacgaa 240
agccatgacc acatggatga tatggatgat gaagatgatg atgaccatgt ggacagccag 300
gactccattg actcgaacga ctctgatgat gtagatgaca ctgatgattc tcaccagtct 360
gatgagtctc accattctga tgaatctgat gaactggtca ctgattttcc cacggacctg 420
ccagcaaccg aagttttcac tccagttgtc cccacagtag acacatatga tggccgaggt 480
gatagtgtgg tttatggact gaggtcaaaa tctaagaagt ttcgcagacc tgacatccag 540
taccctgatg ctacagacga gcacatcacc tcacacatgg aaagcgagga gttgaatggt 600
gcatacaagg ccatccccgt tgcccaggac ctgaacgcgc cttctgattg ggacagccgt 660
gggaaggaca gttatgaaac gagtcagctg gatgaccaga gtgctgaagc ccacagccac 720
aagcagtcca gattatataa gcggaaagct aatgatgaga gcaatgagca ttccgatgtg 780
attgatagtc aggaactttc caaagtcagc cgtgaattcc acagccatga atttcacagc 840
catgaagata tgctggttgt agaccccaaa agtaaggaag aagataaaca cctgaaattt 900
cgtatttctc atgaattaga tagtgcatct tctgaggtca at 942

<210> 227
<211> 314
<212> PRT
<213> Homo sapiens

<400> 227
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
1 5 10 15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
20 25 30
Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
35 40 45
Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Asn Ala Val Ser Ser Glu

```
    50                  55                  60
Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro Ser Lys Ser Asn Glu
65                  70                  75                  80
Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp Asp His
                85                  90                  95
Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp Val Asp
            100                 105                 110
Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser Asp Glu
        115                 120                 125
Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala Thr Glu
    130                 135                 140
Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly Arg Gly
145                 150                 155                 160
Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe Arg Arg
                165                 170                 175
Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu His Ile Thr Ser His
            180                 185                 190
Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro Val Ala
        195                 200                 205
Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys Asp Ser
    210                 215                 220
Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Ala His Ser His
225                 230                 235                 240
Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser Asn Glu
                245                 250                 255
His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser Arg Glu
            260                 265                 270
Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val Val Asp
        275                 280                 285
Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile Ser His
    290                 295                 300
Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
305                 310
```

<210> 228
<211> 1524
<212> DNA
<213> Homo sapiens

<400> 228

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gcagagcaca gcatcgtcgg gaccagactc gtctcaggcc agttgcagcc ttctcagcca 60
aacgccgacc aaggaaaact cactaccatg agaattgcag tgatttgctt ttgcctccta 120
ggcatcacct gtgccatacc agttaaacag gctgattctg gaagttctga ggaaaagcag 180
ctttacaaca aatacccaga tgctgtggcc acatggctaa accctgaccc atctcagaag 240
cagaatctcc tagccccaca gacccttcca agtaagtcca acgaaagcca tgaccacatg 300
gatgatatgg atgatgaaga tgatgatgac catgtggaca gccaggactc cattgactcg 360
aacgactctg atgatgtaga tgacactgat gattctcacc agtctgatga gtctcaccat 420
tctgatgaat ctgatgaact ggtcactgat tttcccacgg acctgccagc aaccgaagtt 480
ttcactccag ttgtccccac agtagacaca tatgatggcc gaggtgatag tgtggtttat 540
ggactgaggt caaaatctaa gaagtttcgc agacctgaca tccagtaccc tgatgctaca 600
gacgaggaca tcacctcaca catggaaagc gaggagttga atggtgcata caaggccatc 660
cccgttgccc aggacctgaa cgcgccttct gattgggaca gccgtgggaa ggacagttat 720
gaaacgagtc agctggatga ccagagtgct gaaacccaca gccacaagca gtccagatta 780
tataagcgga aagccaatga tgagagcaat gagcattccg atgtgattga tagtcaggaa 840
ctttccaaag tcagccgtga attccacagc catgaatttc acagccatga agatatgctg 900
gttgtagacc ccaaaagtaa ggaagaagat aaacacctga aatttcgtat ttctcatgaa 960
ttagatagtg catcttctga ggtcaattaa aaggagaaaa aatacaattt ctcactttgc 1020
```

```
atttagtcaa aagaaaaaat gctttatagc aaaatgaaag agaacatgaa atgcttcttt 1080
ctcagtttat tggttgaatg tgtatctatt tgagtctgga aataactaat gtgtttgata 1140
attagtttag tttgtggctt catggaaact ccctgtaaac taaaagcttc agggttatgt 1200
ctatgttcat tctatagaag aaatgcaaac tatcactgta ttttaatatt tgttattctc 1260
tcatgaatag aaatttatgt agaagcaaac aaaatacttt tacccactta aaaagagaat 1320
ataacatttt atgtcactat aatcttttgt tttttaagtt agtgtatatt ttgttgtgat 1380
tatctttttg tggtgtgaat aaatctttta tcttgaatgt aataagaatt tggtggtgtc 1440
aattgcttat ttgttttccc acggttgtcc agcaattaat aaaacataac ctttttttact 1500
gcctaaaaaa aaaaaaaaaa aaaa                                        1524
```

<210> 229
<211> 300
<212> PRT
<213> Homo sapiens

<400> 229

```
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
 1               5                  10                  15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Leu
            20                  25                  30
Tyr Asn Lys Tyr Pro Asp Ala Val Ala Thr Trp Leu Asn Pro Asp Pro
        35                  40                  45
Ser Gln Lys Gln Asn Leu Leu Ala Pro Gln Thr Leu Pro Ser Lys Ser
    50                  55                  60
Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu Asp Asp Asp
65                  70                  75                  80
Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp Ser Asp Asp
                85                  90                  95
Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser His His Ser
            100                 105                 110
Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp Leu Pro Ala
        115                 120                 125
Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr Tyr Asp Gly
    130                 135                 140
Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser Lys Lys Phe
145                 150                 155                 160
Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu Asp Ile Thr
                165                 170                 175
Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys Ala Ile Pro
            180                 185                 190
Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser Arg Gly Lys
        195                 200                 205
Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala Glu Thr His
    210                 215                 220
Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn Asp Glu Ser
225                 230                 235                 240
Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser Lys Val Ser
                245                 250                 255
Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp Met Leu Val
            260                 265                 270
Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys Phe Arg Ile
        275                 280                 285
Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
    290                 295                 300
```

<210> 230
<211> 861

<212> DNA
<213> Homo sapiens

<400> 230
atgagaattg cagtgatttg cttttgcctc ctaggcatca cctgtgccat accagttaaa 60
caggctgatt ctggaagttc tgaggaaaag cagaatgctg tgtcctctga agaaaccaat 120
gactttaaac aagagaccct tccaagtaag tccaacgaaa gccatgacca catggatgat 180
atggatgatg aagatgatga tgaccatgtg gacagccagg actccattga ctcgaacgac 240
tctgatgatg tagatgacac tgatgattct caccagtctg atgagtctca ccattctgat 300
gaatctgatg aactggtcac tgatttttccc acggacctgc cagcaaccga agttttcact 360
ccagttgtcc ccacagtaga cacatatgat ggccgaggtg atagtgtggt ttatggactg 420
aggtcaaaat ctaagaagtt tcgcagacct gacatccagt accctgatgc tacagacgag 480
cacatcacct cacacatgga aagcgaggag ttgaatggtg catacaaggc catccccgtt 540
gcccaggacc tgaacgcgcc ttctgattgg gacagccgtg ggaaggacag ttatgaaacg 600
agtcagctgg atgaccagag tgctgaagcc cacagccaca agcagtccag attatataag 660
cggaaagcta atgatgagag caatgagcat tccgatgtga ttgatagtca ggaactttcc 720
aaagtcagcc gtgaattcca cagccatgaa tttcacagcc atgaagatat gctggttgta 780
gaccccaaaa gtaaggaaga agataaacac ctgaaatttc gtatttctca tgaattagat 840
agtgcatctt ctgaggtcaa t 861

<210> 231
<211> 287
<212> PRT
<213> Homo sapiens

<400> 231
Met Arg Ile Ala Val Ile Cys Phe Cys Leu Leu Gly Ile Thr Cys Ala
1 5 10 15
Ile Pro Val Lys Gln Ala Asp Ser Gly Ser Ser Glu Glu Lys Gln Asn
20 25 30
Ala Val Ser Ser Glu Glu Thr Asn Asp Phe Lys Gln Glu Thr Leu Pro
35 40 45
Ser Lys Ser Asn Glu Ser His Asp His Met Asp Asp Met Asp Asp Glu
50 55 60
Asp Asp Asp Asp His Val Asp Ser Gln Asp Ser Ile Asp Ser Asn Asp
65 70 75 80
Ser Asp Asp Val Asp Asp Thr Asp Asp Ser His Gln Ser Asp Glu Ser
85 90 95
His His Ser Asp Glu Ser Asp Glu Leu Val Thr Asp Phe Pro Thr Asp
100 105 110
Leu Pro Ala Thr Glu Val Phe Thr Pro Val Val Pro Thr Val Asp Thr
115 120 125
Tyr Asp Gly Arg Gly Asp Ser Val Val Tyr Gly Leu Arg Ser Lys Ser
130 135 140
Lys Lys Phe Arg Arg Pro Asp Ile Gln Tyr Pro Asp Ala Thr Asp Glu
145 150 155 160
His Ile Thr Ser His Met Glu Ser Glu Glu Leu Asn Gly Ala Tyr Lys
165 170 175
Ala Ile Pro Val Ala Gln Asp Leu Asn Ala Pro Ser Asp Trp Asp Ser
180 185 190
Arg Gly Lys Asp Ser Tyr Glu Thr Ser Gln Leu Asp Asp Gln Ser Ala
195 200 205
Glu Ala His Ser His Lys Gln Ser Arg Leu Tyr Lys Arg Lys Ala Asn
210 215 220
Asp Glu Ser Asn Glu His Ser Asp Val Ile Asp Ser Gln Glu Leu Ser
225 230 235 240
Lys Val Ser Arg Glu Phe His Ser His Glu Phe His Ser His Glu Asp
245 250 255

```
Met Leu Val Val Asp Pro Lys Ser Lys Glu Glu Asp Lys His Leu Lys
            260                 265                 270
Phe Arg Ile Ser His Glu Leu Asp Ser Ala Ser Ser Glu Val Asn
        275                 280                 285


<210> 232
<211> 838
<212> DNA
<213> Homo sapiens

<400> 232
ctcagagcca cccacagccg cagccatgct gtgcctcctg ctcaccctgg gcgtggccct 60
ggtctgtggt gtcccggcca tggacatccc ccagaccaag caggacctgg agctcccaaa 120
gttggcaggg acctggcact ccatggccat ggcgaccaac aacatctccc tcatggcgac 180
actgaaggcc cctctgaggg tccacatcac ctcactgttg cccacccccg aggacaacct 240
ggagatcgtt ctgcacagat gggagaacaa cagctgtgtt gagaagaagg tccttggaga 300
gaagactgag aatccaaaga agttcaagat caactatacg gtggcgaacg aggccacgct 360
gctcgatact gactacgaca atttcctgtt tctctgccta caggacacca ccacccccat 420
ccagagcatg atgtgccagt acctggccag agtcctggtg gaggacgatg agatcatgca 480
gggattcatc agggctttca ggcccctgcc caggcaccta tggtacttgc tggacttgaa 540
acagatggaa gagccgtgcc gtttctaggt gagctcctgc ctggtcctgc ctcctggctc 600
acctccgcct ccaggaagac cagactccca cccttccaca cctccagagc agtgggactt 660
cctcctgccc tttcaaagaa taaccacagc tcagaagacg atgacgtggt catctgtgtc 720
gccatcccct tcctgctgca cacctgcacc acggccatgg ggaggctgct ccctgggggc 780
agagtctctg gcagaggtta ttaataaacc cttggagcat gaaaaaaaaa aaaaaaa   838

<210> 233
<211> 180
<212> PRT
<213> Homo sapiens

<400> 233
Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
1               5                   10                  15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
            20                  25                  30
Leu Ala Gly Thr Trp His Ser Met Ala Met Ala Thr Asn Asn Ile Ser
        35                  40                  45
Leu Met Ala Thr Leu Lys Ala Pro Leu Arg Val His Ile Thr Ser Leu
    50                  55                  60
Leu Pro Thr Pro Glu Asp Asn Leu Glu Ile Val Leu His Arg Trp Glu
65                  70                  75                  80
Asn Asn Ser Cys Val Glu Lys Lys Val Leu Gly Glu Lys Thr Glu Asn
                85                  90                  95
Pro Lys Lys Phe Lys Ile Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu
            100                 105                 110
Leu Asp Thr Asp Tyr Asp Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr
        115                 120                 125
Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg Val Leu
    130                 135                 140
Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe Arg Pro
145                 150                 155                 160
Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu
                165                 170                 175
Pro Cys Arg Phe
            180
```

<210> 234
<211> 851
<212> DNA
<213> Homo sapiens

<400> 234
ggctccagag ctcagagcca cccacagccg cagccatgct gtgcctcctg ctcaccctgg 60
gcgtggccct ggtctgtggt gtcccggcca tggacatccc ccagaccaag caggacctgg 120
agctcccaaa gttggcaggg acctggcact ccatggccat ggcgaccaac aacatctccc 180
tcatggcgac actgaaggcc cctctgaggg tccacatcac ctcactgttg cccacccccg 240
aggacaacct ggagatcgtt ctgcacagat gggagaacaa cagctgtgtt gagaagaagg 300
tccttggaga gaagactgag aatccaaaga agttcaagat caactatacg gtggcgaacg 360
aggccacgct gctcgatact gactacgaca atttcctgtt tctctgccta caggacacca 420
ccacccccat ccagagcatg atgtgccagt acctggccag agtcctggtg gaggacgatg 480
agatcatgca gggattcatc agggctttca ggcccctgcc caggcaccta tggtacttgc 540
tggacttgaa acagatggaa gagccgtgcc gtttctaggt gagctcctgc ctggtcctgc 600
ctcctgggtg acctgtaaac ccaacagctc acctccgcct ccaggaagac cagactccca 660
cccttccaca cctccagagc agtgggactt cctcctgccc tttcaaagaa taaccacagc 720
tcagaagacg atgacgtggt catctgtgtc gccatcccct tcctgctgca cacctgcacc 780
acggccatgg ggaggctgct ccctgggggc agagtctctg gcagaggtta ttaataaacc 840
cttggagcat g 851

<210> 235
<211> 811
<212> DNA
<213> Homo sapiens

<400> 235
catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60
tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120
aggacctgga gctcccaaag ttggcaggga cctggcactc catggccatg gcgaccaaca 180
acatctccct catggcgaca ctgaaggccc ctctgagggt ccacatcacc tcactgttgc 240
ccacccccga ggacaacctg gagatcgttc tgcacagatg ggagaacaac agctgtgttg 300
agaagaaggt ccttggagag aagactggga atccaaagaa gttcaagatc aactatacgg 360
tggcgaacga ggccacgctg ctcgatactg actacgacaa tttcctgttt ctctgcctac 420
aggacaccac cacccccatc cagagcatga tgtgccagta cctggccaga gtcctggtgg 480
aggacgatga gatcatgcag ggattcatca gggctttcag gcccctgccc aggcacctat 540
ggtacttgct ggacttgaaa cagatggaag agccgtgccg tttctagctc acctccgcct 600
ccaggaagac cagactccca cccttccaca cctccagagc agtgggactt cctcctgccc 660
tttcaaagaa taaccacagc tcagaagacg atgacgtggt catctgtgtc gccatcccct 720
tcctgctgca cacctgcacc attgccatgg ggaggctgct ccctgggggc agagtctctg 780
gcagaggtta ttaataaacc cttggagcat g 811

<210> 236
<211> 850
<212> DNA
<213> Homo sapiens

<400> 236
catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60
tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120
aggacctgga gctcccaaag ttggcaggga cctggcactc catggccatg gcgaccaaca 180
acatctccct catggcgaca ctgaaggccc ctctgagggt ccacatcacc tcactgttgc 240
ccacccccga ggacaacctg gagatcgttc tgcacagatg ggagaacaac agctgtgttg 300
agaagaaggt ccttggagag aagactgrga atccaaagaa gttcaagatc aactatacgg 360
tggcgaacga ggccacgctg ctcgatactg actacgacaa tttcctgttt ctctgcctac 420
aggacaccac cacccccatc cagagcatga tgtgccagta cctggccaga gtcctggtgg 480

```
aggacgatga gatcatgcag ggattcatca gggctttcag gcccctgccc aggcacctat 540
ggtacttgct ggacttgaaa cagatggaag agccgtgccg tttctagtga cctgtaaacc 600
caacagctca cctccgcctc caggaagacc agactcccac ccttccacac ctccagagca 660
gtgggacttc ctcctgccct ttcaaagaat aaccacagct cagaagacga tgacgtggtc 720
atctgtgtcg ccatcccctt cctgctgcac acctgcacca cggccatggg gaggctgctc 780
cctgggggca gagtctctgg cagaggttat taataaaccc ttggagcatg aaaaaaaaaa 840
aaaaaaaaaa                                                        850
```

<210> 237
<211> 598
<212> DNA
<213> Homo sapiens

<400> 237

```
catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60
tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120
aggacctgga gctcccaaag gacaccacca cccccatcca gagcatgatg tgccagtacc 180
tggccagagt cctggtggag gacgatgaga tcatgcaggg attcatcagg gctttcaggc 240
ccctgcccag gcacctatgg tacttgctgg acttgaaaca gatggaagag ccgtgccgtt 300
tctaggtgag ctcctgcctg gtcctgcctc ctgggtgacc tgtaaaccca acagctcacc 360
tccgcctcca ggaagaccag actcccaccc ttccacacct ccagagcagt gggacttcct 420
cctgcccttt caaagaataa ccacagctca gaagacgatg acgtggtcat ctgtgtcgcc 480
atccccttcc tgctgcacac ctgcaccacg gccatgggga ggctgctccc tgggggcaga 540
gtctctggca gaggttatta ataaaccctt ggagcatgaa aaaaaaaaaa aaaaaaa    598
```

<210> 238
<211> 86
<212> PRT
<213> Homo sapiens

<400> 238

```
Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
 1               5                  10                  15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
            20                  25                  30
Asp Thr Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg
        35                  40                  45
Val Leu Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe
    50                  55                  60
Arg Pro Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met
65                  70                  75                  80
Glu Glu Pro Cys Arg Phe
                85
```

<210> 239
<211> 814
<212> DNA
<213> Homo sapiens

<400> 239

```
catccctctg gctccagagc tcagagccac ccacagccgc agccatgctg tgcctcctgc 60
tcaccctggg cgtggccctg gtctgtggtg tcccggccat ggacatcccc cagaccaagc 120
aggacctgga gacactgaag gcccctctga gggtccacat cacctcactg ttgcccaccc 180
ccgaggacaa cctggagatc gttctgcaca gatgggagaa caacagctgt gttgagaaga 240
aggtccttgg agagaagact grgaatccaa agaagttcaa gatcaactat acggtggcga 300
acgaggccac gctgctcgat actgactacg acaatttcct gtttctctgc ctacaggaca 360
ccaccacccc catccagagc atgatgtgcc agtacctggc cagagtcctg gtggaggacg 420
```

```
atgagatcat gcagggattc atcagggctt tcaggcccct gcccaggcac ctatggtact 480
tgctggactt gaaacagatg gaagagccgt gccgtttcta ggtgagctcc tgcctggtcc 540
tgcctcctgg gtgacctgta aacccaacag ctcacctccg cctccaggaa gaccagactc 600
ccacccttcc acacctccag agcagtggga cttcctcctg ccctttcaaa gaataaccac 660
agctcagaag acgatgacgt ggtcatctgt gtcgccatcc ccttcctgct gcacacctgc 720
accacggcca tggggaggct gctccctggg ggcagagtct ctggcagagg ttattaataa 780
acccttggag catgaaaaaa aaaaaaaaaa aaaa                             814
```

<210> 240
<211> 158
<212> PRT
<213> Homo sapiens

<400> 240

```
Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
1               5                   10                  15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
            20                  25                  30
Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro Thr Pro Glu Asp
        35                  40                  45
Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn Ser Cys Val Glu
    50                  55                  60
Lys Lys Val Leu Gly Glu Lys Thr Glu Asn Pro Lys Lys Phe Lys Ile
65                  70                  75                  80
Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp Thr Asp Tyr Asp
                85                  90                  95
Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr Pro Ile Gln Ser
            100                 105                 110
Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu Asp Asp Glu Ile
        115                 120                 125
Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro Arg His Leu Trp
    130                 135                 140
Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys Arg Phe
145                 150                 155
```

<210> 241
<211> 158
<212> PRT
<213> Homo sapiens

<400> 241

```
Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
1               5                   10                  15
Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Thr Leu Lys
            20                  25                  30
Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro Thr Pro Glu Asp
        35                  40                  45
Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn Ser Cys Val Glu
    50                  55                  60
Lys Lys Val Leu Gly Glu Lys Thr Glu Asn Pro Lys Lys Phe Lys Ile
65                  70                  75                  80
Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp Thr Asp Tyr Asp
                85                  90                  95
Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr Pro Ile Gln Ser
            100                 105                 110
Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu Asp Asp Glu Ile
        115                 120                 125
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Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro Arg His Leu Trp
    130                 135                 140
Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys Arg Phe
145                 150                 155


<210> 242
<211> 2707
<212> DNA
<213> Homo sapiens

<400> 242
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ggaggaagcc ccgagccctc ggcgggctgc gagcgactcc ccggcgatgc ctcacaactc 180
catcagatct ggccatggag ggctgaacca gctgggaggg gcctttgtga atggcagacc 240
tctgccggaa gtggtccgcc agcgcatcgt agacctggcc caccagggtg taaggccctg 300
cgacatctct cgccagctcc gcgtcagcca tggctgcgtc agcaagatcc ttggcaggta 360
ctacgagact ggcagcatcc ggcctggagt gataggggc tccaagccca aggtggccac 420
ccccaaggtg gtggagaaga ttggggacta caaacgccag aaccctacca tgtttgcctg 480
ggagatccga gaccggctcc tggctgaggg cgtctgtgac aatgacactg tgcccagtgt 540
cagctccatt aatagaatca tccggaccaa agtgcagcaa ccattcaacc tccctatgga 600
cagctgcgtg gccaccaagt ccctgagtcc cggacacacg ctgatcccca gctcagctgt 660
aactcccccg gagtcacccc agtcggattc cctgggctcc acctactcca tcaatgggct 720
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cgccataaag caggaaaccc ccgaggtgtc cagttctagc tccacccctt cctctttatc 1140
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tccccatgct gcctccgtgt acgggcagtt cacgggccag gccctcctct cagggcgaga 1260
gatggtgggg cccacgctgc ccggataccc accccacatc ccccaccagcg gacagggcag 1320
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tcagcctggg acaggcccca gagagtcaca caaaggaatc tttatttatt acatgaaaaa 1620
taaccacaag tccagcattg cggcacactc cctgtgtggt taatttaatg aaccatgaaa 1680
gacaggatga ccttggacaa ggccaaactg tcctccaaga ctccttaatg aggggcagga 1740
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cacaactcta gcaattatgg accataagca cttccctcca gcccacaagt cacagcctgg 1980
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gcttcctgca gctcacgccc accagctact gaagggaccc aaggcacccc ctgaagccag 2460
cgatagaggg tccctctctg ctccccagca gctcctgccc ccaaggcctg actgtatata 2520
ctgtcaatga aactttgttt gggtcaagct tccttctttc taccccccag actttggcct 2580
ctgagtgaaa tgtctctctt tgccctgtgg ggcttctctc cttgatgctt ctttcttttt 2640
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<210> 243
<211> 450
<212> PRT
<213> Homo sapiens

<400> 243
Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
1 5 10 15
Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
20 25 30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
35 40 45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
50 55 60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65 70 75 80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
85 90 95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
100 105 110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
115 120 125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
130 135 140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145 150 155 160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
165 170 175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
180 185 190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
195 200 205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
210 215 220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225 230 235 240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
245 250 255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
260 265 270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
275 280 285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Asp Pro His Ser Pro
290 295 300
Phe Ala Ile Lys Gln Glu Thr Pro Glu Val Ser Ser Ser Ser Ser Thr
305 310 315 320
Pro Ser Ser Leu Ser Ser Ser Ala Phe Leu Asp Leu Gln Gln Val Gly
325 330 335
Ser Gly Val Pro Pro Phe Asn Ala Phe Pro His Ala Ala Ser Val Tyr
340 345 350
Gly Gln Phe Thr Gly Gln Ala Leu Leu Ser Gly Arg Glu Met Val Gly
355 360 365
Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln Gly
370 375 380
Ser Tyr Ala Ser Ser Ala Ile Ala Gly Met Val Ala Gly Ser Glu Tyr
385 390 395 400
Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu Ala

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                405                 410                 415
Trp Arg Phe Pro Asn Ser Ser Leu Leu Ser Ser Pro Tyr Tyr Tyr Ser
            420                 425                 430
Ser Thr Ser Arg Pro Ser Ala Pro Pro Thr Thr Ala Thr Ala Phe Asp
        435                 440                 445
His Leu
    450
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<210> 244
<211> 2381
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(2381)
<223> n = A,T,C or G

<400> 244

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ggcccaccag ggtgtaaggc cctgcgacat ctctcgccag ctccgcgtca gccatggttg 180
cgtcagcaag atccttggca ggtactacga gactggcagc atccggcctg gagtgatagg 240
gggctccaag cccaaggtgg ccaccccccaa ggtggtggag aagattgggg actacaaacg 300
ccagaaccct accatgtttg cctgggagat ccgagaccgg ctcctggctg agggcgtctg 360
tgacaatgac actgtgccca gtgtcagctc cattaataga atcatccgga ccaaagtgca 420
gcaaccattc aacctcccta tggacagctg cgtggccacc aagtccctga gtcccggaca 480
cacgctgatc cccagctcag ctgtaactcc cccggagtca ccccagtcgg attccctggg 540
ctccacctac tccatcaatg ggctcctggg catcgctcag cctggcagcg acaagaggaa 600
aatggatgac agtgatcagg atagctgccg actaagcatt gactcacaga gcagcagcag 660
cggaccccga aagcaccttc gcacggatgc cttcagccag caccacctcg agccgctcga 720
gtgcccattt gagcggcagc actacccaga ggcctatgcc tcccccagcc acaccaaagg 780
cgagcagggc ctctacccgc tgcccttgct caacagcacc ctggacgacg ggaaggccac 840
cctgacccct tccaacacgc cactggggcg caacctctcg actcaccaga cctaccccgt 900
ggtggcaggg cgagagatgg tggggcccac gctgcccgga tacccacccc acatccccac 960
cagcggacag ggcagctatg cctcctctgc catcgcaggc atggtggcag gaagtgaata 1020
ctctggcaat gcctatggcc acacccccta ctcctcctac agcgaggcct ggggcttccc 1080
caactccagc ttgctgagtt ccccatatta ttacagttcc acatcaaggc cgagtgcacc 1140
gcccaccact gccacggcct ttgaccatct gtagttgcca tggggacagt gggagcgact 1200
gagcaacagg aggactcagc ctgggacagg ccccagagag tcacacaaag gaatctttat 1260
tattacatga aaaataacca caagtccagc attgcggcac actccctgtg tggttaattt 1320
aatgaaccat gaaagacagg atgaccttgg acaaggccaa actgtcctcc aagactcctt 1380
aatgaggggc aggagtccca gggaaagaga accatgccat gctgaaaaag acaaaattga 1440
agaagaaatg tagccccagc cggtaccctc caaaggagag aagaagcaat agccgaggaa 1500
cttgggggga tggcgaatgg ttcctgcccg ggcccaaggg tgcacagggc acctccatgg 1560
ctccattatt aacacaactc tagcaattat ggaccataag cacttccctc cagcccacaa 1620
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aaaacagaca ttccacaggg cctgggcccc tgggaggtga ggtgtggtgt gcggcttcac 1980
ccagggcaga acaaggcaga atcgcaggaa acccgcnttc cccttcctga cagctcctgc 2040
caagccaaat gtgcttcctg cagctcacgc ccaccangct actgaaggga cccaaggcac 2100
ccccnntgaa gccagcgata gangggtccc tctctgcntc cccagcagct cctgcccccca 2160
naggcctgac tgtatatact gtaaatgaaa ctttgtttgg gtcaagcttc cttctttcta 2220
acccccnaga ctttggcctc tgagtgaaat gtctctcttt gccctgtggg gcttctctcc 2280
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tgctcttcaa aaaaaaaaa aaaaaaaaa aaaaaaaaa a                      2381

<210> 245
<211> 387
<212> PRT
<213> Homo sapiens

<400> 245
Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
1               5                   10                  15
Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
            20                  25                  30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
        35                  40                  45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
    50                  55                  60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65                  70                  75                  80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
                85                  90                  95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
            100                 105                 110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
        115                 120                 125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
    130                 135                 140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145                 150                 155                 160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
                165                 170                 175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
            180                 185                 190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
        195                 200                 205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
    210                 215                 220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225                 230                 235                 240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
                245                 250                 255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
            260                 265                 270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
        275                 280                 285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Gly Arg Glu Met Val
    290                 295                 300
Gly Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln
305                 310                 315                 320
Gly Ser Tyr Ala Ser Ser Ala Ile Ala Gly Met Val Ala Gly Ser Glu
                325                 330                 335
Tyr Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu
            340                 345                 350
Ala Trp Arg Phe Pro Asn Ser Ser Leu Leu Ser Ser Pro Tyr Tyr Tyr
        355                 360                 365
Ser Ser Thr Ser Arg Pro Ser Ala Pro Pro Thr Thr Ala Thr Ala Phe
    370                 375                 380
Asp His Leu
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385

<210> 246
<211> 387
<212> PRT
<213> Homo sapiens

<400> 246
Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
1 5 10 15
Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
20 25 30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
35 40 45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
50 55 60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65 70 75 80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
85 90 95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
100 105 110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
115 120 125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
130 135 140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145 150 155 160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
165 170 175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
180 185 190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
195 200 205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
210 215 220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225 230 235 240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
245 250 255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
260 265 270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
275 280 285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Gly Arg Glu Met Val
290 295 300
Gly Pro Thr Leu Pro Gly Tyr Pro Pro His Ile Pro Thr Ser Gly Gln
305 310 315 320
Gly Ser Tyr Ala Ser Ser Ala Ile Ala Gly Met Val Ala Gly Ser Glu
325 330 335
Tyr Ser Gly Asn Ala Tyr Gly His Thr Pro Tyr Ser Ser Tyr Ser Glu
340 345 350
Ala Trp Gly Phe Pro Asn Ser Ser Leu Leu Ser Ser Pro Tyr Tyr Tyr
355 360 365
Ser Ser Thr Ser Arg Pro Ser Ala Pro Pro Thr Thr Ala Thr Ala Phe
370 375 380
Asp His Leu

385

<210> 247
<211> 2641
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(2641)
<223> n = A,T,C or G

<400> 247
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agccccgagc cctcggcggg ctgcgagcga ctccccggcg atgcctcaca actccatcag 180
atctggccat ggagggctga accagctggg aggggccttt gtgaatggca gacctctgcc 240
ggaagtggtc cgccagcgca tcgtagacct ggcccaccag ggtgtaaggc cctgcgacat 300
ctctcgccag ctccgcgtca gccatggctg cgtcagcaag atccttggca ggtactacga 360
gactggcagc atccggcctg gagtgatagg gggctccaag cccaaggtgg ccaccccccaa 420
ggtggtggag aagattgggg actacaaacg ccagaaccct accatgtttg cctgggagat 480
ccgagaccgg ctcctggctg agggcgtctg tgacaatgac actgtgccca gtgtcagctc 540
cattaataga atcatccgga ccaaagtgca gcaaccattc aacctcccta tggacagctg 600
cgtggccacc aagtccctga gtcccggaca cacgctgatc cccagctcag ctgtaactcc 660
cccggagtca ccccagtcgg attccctggg ctccacctac tccatcaatg ggctcctggg 720
catcgctcag cctggcagcg acaagaggaa aatggatgac agtgatcagg atagctgccg 780
actaagcatt gactcacaga gcagcagcag cggaccccga aagcaccttc gcacggatgc 840
cttcagccag caccacctcg agccgctcga gtgcccattt gagcggcagc actacccaga 900
ggcctatgcc tcccccagcc acaccaaagg cgagcagggc ctctacccgc tgcccttgct 960
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caacctctcg actcaccaga cctaccccgt ggtggcagct ccgccctttt ggatctgcag 1080
caagtcggct ccggggtccc gcccttcaat gcctttcccc atgctgcctc cgtgtacggg 1140
cagttcacgg gccaggccct cctctcaggg cgagagatgg tggggcccac gctgcccgga 1200
tacccacccc acatccccac cagcggacag ggcagctatg cctcctctgc catcgcaggc 1260
atggtggcag gaagtgaata ctctggcaat gcctatggcc acacccccta ctcctcctac 1320
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actccctgtg tggttaattt aatgaaccat gaaagacagg atgaccttgg acaaggccaa 1620
actgtcctcc aagactcctt aatgaggggc aggagtccca gggaaagaga accatgccat 1680
gctgaaaaag acaaaattga agaagaaatg tagccccagc cggtaccctc caaaggagag 1740
aagaagcaat agccgaggaa cttgggggga tggcgaatgg ttcctgcccg ggcccaaggg 1800
tgcacagggc acctccatgg ctccattatt aacacaactc tagcaattat ggaccataag 1860
cacttccctc cagcccacaa gtcacagcct ggtgccgagg ctctgctcac cagccaccca 1920
gggagtcacc tccctcagcc tcccgcctgc cccacacgga ggctctggct gtcctctttc 1980
ctccactcca tttgcttggc tctttctaca cctccctctt ggatgggctg agggctggag 2040
cgagtccctc agaaattcca ccaggctgtc agctgacctc tttttcctgc tgctgtgaag 2100
gtatagcacc ancccaggtc ctcctgcagt gcggcatccc cttggcagct gccgtcagcc 2160
aggccagccc cagggagctt aaaacagaca ttccacaggg cctgggcccc tgggaggtga 2220
ggtgtggtgt gcggcttcac ccagggcaga acaaggcaga atcgcaggaa acccgcnttc 2280
cccttcctga cagctcctgc caagccaaat gtgcttcctg cagctcacgc ccaccangct 2340
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cccagcagct cctgccccca naggcctgac tgtatatact gtaaatgaaa ctttgtttgg 2460
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gccctgtggg gcttctctcc ttgatgcttc tttcttttt taaagacaac ctgccattac 2580
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<210> 248
<211> 398
<212> PRT
<213> Homo sapiens

<400> 248
Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
1               5                   10                  15
Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
            20                  25                  30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
        35                  40                  45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
    50                  55                  60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65                  70                  75                  80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
                85                  90                  95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
            100                 105                 110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
        115                 120                 125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
    130                 135                 140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145                 150                 155                 160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
                165                 170                 175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
            180                 185                 190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
        195                 200                 205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
    210                 215                 220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225                 230                 235                 240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
                245                 250                 255
Gly Glu Gln Gly Leu Tyr Pro Leu Pro Leu Leu Asn Ser Thr Leu Asp
            260                 265                 270
Asp Gly Lys Ala Thr Leu Thr Pro Ser Asn Thr Pro Leu Gly Arg Asn
        275                 280                 285
Leu Ser Thr His Gln Thr Tyr Pro Val Val Ala Ala Pro Pro Phe Trp
    290                 295                 300
Ile Cys Ser Lys Ser Ala Pro Gly Ser Arg Pro Ser Met Pro Phe Pro
305                 310                 315                 320
Met Leu Pro Pro Cys Thr Gly Ser Ser Arg Ala Arg Pro Ser Ser Gln
                325                 330                 335
Gly Glu Arg Trp Trp Gly Pro Arg Cys Pro Asp Thr His Pro Thr Ser
            340                 345                 350
Pro Pro Ala Asp Arg Ala Ala Met Pro Pro Leu Pro Ser Gln Ala Trp
        355                 360                 365
Trp Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr Pro Pro Thr
    370                 375                 380
Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala Cys
385                 390                 395
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<210> 249
<211> 2410
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(2410)
<223> n = A,T,C or G

<400> 249
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<210> 250
<211> 321
<212> PRT

<213> Homo sapiens

<400> 250
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20 25 30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
35 40 45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
50 55 60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65 70 75 80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
85 90 95
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
100 105 110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
115 120 125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
130 135 140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145 150 155 160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
165 170 175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
180 185 190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
195 200 205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
210 215 220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225 230 235 240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
245 250 255
Gly Glu Gln Gly Glu Arg Trp Trp Gly Pro Arg Cys Pro Asp Thr His
260 265 270
Pro Thr Ser Pro Pro Ala Asp Arg Ala Ala Met Pro Pro Leu Pro Ser
275 280 285
Gln Ala Trp Trp Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr
290 295 300
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Cys

<210> 251
<211> 2308
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(2308)
<223> n = A,T,C or G

<400> 251

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ggaagtggtc cgccagcgca tcgtagacct ggcccaccag ggtgtaaggc cctgcgacat 300
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ccgagaccgg ctcctggctg agggcgtctg tgacaatgac actgtgccca gtgtcagctc 540
cattaataga atcatccgga ccaaagtgca gcaaccattc aacctcccta tggacagctg 600
cgtggccacc aagtccctga gtcccggaca cacgctgatc ccccagctcag ctgtaactcc 660
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tggcctctga gtgaaatgtc tctctttgcc ctgtggggct tctctccttg atgcttcttt 2220
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aaaaaaaaaa aaaaaaaaaa aaaaaaaa                                     2308
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<210> 252
<211> 287
<212> PRT
<213> Homo sapiens

<400> 252
Met Pro His Asn Ser Ile Arg Ser Gly His Gly Gly Leu Asn Gln Leu
 1               5                   10                  15
Gly Gly Ala Phe Val Asn Gly Arg Pro Leu Pro Glu Val Val Arg Gln
            20                  25                  30
Arg Ile Val Asp Leu Ala His Gln Gly Val Arg Pro Cys Asp Ile Ser
        35                  40                  45
Arg Gln Leu Arg Val Ser His Gly Cys Val Ser Lys Ile Leu Gly Arg
    50                  55                  60
Tyr Tyr Glu Thr Gly Ser Ile Arg Pro Gly Val Ile Gly Gly Ser Lys
65                  70                  75                  80
Pro Lys Val Ala Thr Pro Lys Val Val Glu Lys Ile Gly Asp Tyr Lys
                85                  90                  95
```

```
Arg Gln Asn Pro Thr Met Phe Ala Trp Glu Ile Arg Asp Arg Leu Leu
            100                 105                 110
Ala Glu Gly Val Cys Asp Asn Asp Thr Val Pro Ser Val Ser Ser Ile
        115                 120                 125
Asn Arg Ile Ile Arg Thr Lys Val Gln Gln Pro Phe Asn Leu Pro Met
    130                 135                 140
Asp Ser Cys Val Ala Thr Lys Ser Leu Ser Pro Gly His Thr Leu Ile
145                 150                 155                 160
Pro Ser Ser Ala Val Thr Pro Pro Glu Ser Pro Gln Ser Asp Ser Leu
                165                 170                 175
Gly Ser Thr Tyr Ser Ile Asn Gly Leu Leu Gly Ile Ala Gln Pro Gly
            180                 185                 190
Ser Asp Lys Arg Lys Met Asp Asp Ser Asp Gln Asp Ser Cys Arg Leu
        195                 200                 205
Ser Ile Asp Ser Gln Ser Ser Ser Ser Gly Pro Arg Lys His Leu Arg
    210                 215                 220
Thr Asp Ala Phe Ser Gln His His Leu Glu Pro Leu Glu Cys Pro Phe
225                 230                 235                 240
Glu Arg Gln His Tyr Pro Glu Ala Tyr Ala Ser Pro Ser His Thr Lys
                245                 250                 255
Gly Glu Gln Glu Val Asn Thr Leu Ala Met Pro Met Ala Thr Pro Pro
            260                 265                 270
Thr Pro Pro Thr Ala Arg Pro Gly Ala Ser Pro Thr Pro Ala Cys
        275                 280                 285
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<210> 253
<211> 2148
<212> DNA
<213> Homo sapiens

<400> 253

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gagacctaga aatccaagcg ttggaggtcc tgaggccagc ctaagtcgct tcaaaatgga 240
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cccacggaga cttgtggagc tggcagggca gagcctgctg aaggatgagg ccctggccat 360
tgccgccctg gagttgctgc ccagggagct cttcccgcca ctcttcatgg cagcctttga 420
cgggagacac agccagaccc tgaaggcaat ggtgcaggcc tggcccttca cctgcctccc 480
tctgggagtg ctgatgaagg gacaacatct tcacctggag accttcaaag ctgtgcttga 540
tggacttgat gtgctccttg cccaggaggt tcgccccagg aggtggaaac ttcaagtgct 600
ggatttacgg aagaactctc atcaggactt ctggactgta tggtctggaa acagggccag 660
tctgtactca tttccagagc cagaagcagc tcagcccatg acaaagaagc gaaaagtaga 720
tggtttgagc acagaggcag agcagccctt cattccagta gaggtgctcg tagacctgtt 780
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ccccttggaa accctctcaa taactaactg ccggctttcg gaaggggatg tgatgcatct 1260
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```

```
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tagtgccaac ccctgtcctc actgtgggga cagaaccttc tatgacccgg agcccatcct 1740
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acaaatgttc agtgtgagtg aggaaaacat gttcagtgag gaaaaaacat tcagacaaat 1920
gttcagtgag gaaaaaaagg ggaagttggg gataggcaga tgttgacttg aggagttaat 1980
gtgatctttg gggagataca tcttatagag ttagaaatag aatctgaatt tctaaaggga 2040
gattctggct tgggaagtac atgtaggagt taatccctgt gtagactgtt gtaaagaaac 2100
tgttgaaaat aaagagaagc aatgtgaagc aaaaaaaaaa aaaaaaa              2148
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<210> 254
<211> 509
<212> PRT
<213> Homo sapiens

<400> 254

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Met Glu Arg Arg Arg Leu Trp Gly Ser Ile Gln Ser Arg Tyr Ile Ser
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Met Ser Val Trp Thr Ser Pro Arg Arg Leu Val Glu Leu Ala Gly Gln
            20                  25                  30
Ser Leu Leu Lys Asp Glu Ala Leu Ala Ile Ala Ala Leu Glu Leu Leu
        35                  40                  45
Pro Arg Glu Leu Phe Pro Pro Leu Phe Met Ala Ala Phe Asp Gly Arg
    50                  55                  60
His Ser Gln Thr Leu Lys Ala Met Val Gln Ala Trp Pro Phe Thr Cys
65                  70                  75                  80
Leu Pro Leu Gly Val Leu Met Lys Gly Gln His Leu His Leu Glu Thr
                85                  90                  95
Phe Lys Ala Val Leu Asp Gly Leu Asp Val Leu Leu Ala Gln Glu Val
            100                 105                 110
Arg Pro Arg Arg Trp Lys Leu Gln Val Leu Asp Leu Arg Lys Asn Ser
        115                 120                 125
His Gln Asp Phe Trp Thr Val Trp Ser Gly Asn Arg Ala Ser Leu Tyr
    130                 135                 140
Ser Phe Pro Glu Pro Glu Ala Ala Gln Pro Met Thr Lys Lys Arg Lys
145                 150                 155                 160
Val Asp Gly Leu Ser Thr Glu Ala Glu Gln Pro Phe Ile Pro Val Glu
                165                 170                 175
Val Leu Val Asp Leu Phe Leu Lys Glu Gly Ala Cys Asp Glu Leu Phe
            180                 185                 190
Ser Tyr Leu Ile Glu Lys Val Lys Arg Lys Lys Asn Val Leu Arg Leu
        195                 200                 205
Cys Cys Lys Lys Leu Lys Ile Phe Ala Met Pro Met Gln Asp Ile Lys
    210                 215                 220
Met Ile Leu Lys Met Val Gln Leu Asp Ser Ile Glu Asp Leu Glu Val
225                 230                 235                 240
Thr Cys Thr Trp Lys Leu Pro Thr Leu Ala Lys Phe Ser Pro Tyr Leu
                245                 250                 255
Gly Gln Met Ile Asn Leu Arg Arg Leu Leu Leu Ser His Ile His Ala
            260                 265                 270
Ser Ser Tyr Ile Ser Pro Glu Lys Glu Glu Gln Tyr Ile Ala Gln Phe
        275                 280                 285
Thr Ser Gln Phe Leu Ser Leu Gln Cys Leu Gln Ala Leu Tyr Val Asp
    290                 295                 300
Ser Leu Phe Phe Leu Arg Gly Arg Leu Asp Gln Leu Leu Arg His Val
305                 310                 315                 320
Met Asn Pro Leu Glu Thr Leu Ser Ile Thr Asn Cys Arg Leu Ser Glu
```

```
                325                     330                     335
Gly Asp Val Met His Leu Ser Gln Ser Pro Ser Val Ser Gln Leu Ser
            340                     345                     350
Val Leu Ser Leu Ser Gly Val Met Leu Thr Asp Val Ser Pro Glu Pro
        355                     360                     365
Leu Gln Ala Leu Leu Glu Arg Ala Ser Ala Thr Leu Gln Asp Leu Val
    370                     375                     380
Phe Asp Glu Cys Gly Ile Thr Asp Asp Gln Leu Leu Ala Leu Leu Pro
385                     390                     395                     400
Ser Leu Ser His Cys Ser Gln Leu Thr Thr Leu Ser Phe Tyr Gly Asn
                405                     410                     415
Ser Ile Ser Ile Ser Ala Leu Gln Ser Leu Leu Gln His Leu Ile Gly
            420                     425                     430
Leu Ser Asn Leu Thr His Val Leu Tyr Pro Val Pro Leu Glu Ser Tyr
        435                     440                     445
Glu Asp Ile His Gly Thr Leu His Leu Glu Arg Leu Ala Tyr Leu His
    450                     455                     460
Ala Arg Leu Arg Glu Leu Leu Cys Glu Leu Gly Arg Pro Ser Met Val
465                     470                     475                     480
Trp Leu Ser Ala Asn Pro Cys Pro His Cys Gly Asp Arg Thr Phe Tyr
                485                     490                     495
Asp Pro Glu Pro Ile Leu Cys Pro Cys Phe Met Pro Asn
            500                     505
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<210> 255
<211> 2261
<212> DNA
<213> Homo sapiens

<400> 255

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cgcccgaagc gccccccgca cccccggcct ccagcgttga ggcgggggag tgaggagatg 180
ccgacccaga gggacagcag caccatgtcc cacacggtcg caggcggcgg cagcggggac 240
cattcccacc aggtccgggt gaaagcctac taccgcgggg atatcatgat aacacatttt 300
gaaccttcca tctcctttga gggcctttgc aatgaggttc gagacatgtg ttcttttgac 360
aacgaacagc tcttcaccat gaaatggata gatgaggaag gagacccgtg tacagtatca 420
tctcagttgg agttagaaga agcctttaga ctttatgagc taaacaagga ttctgaactc 480
ttgattcatg tgttcccttg tgtaccagaa cgtcctggga tgccttgtcc aggagaagat 540
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actttccaag ccaagcgttt caacaggcgt gctcactgtg ccatctgcac agaccgaata 660
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tgccataaac tcgtcacaat tgaatgtggg cggcattctt tgccacagga accagtgatg 780
cccatggatc agtcatccat gcattctgac catgcacaga cagtaattcc atataatcct 840
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tccagacaat catgtcaaaa tttagttgaa ctggtttttc agtttttaaa aggcctacag 2220
atgagtaatg aagttacctt ttttgtttaa aaaaaaaaaa g                     2261
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<210> 256
<211> 587
<212> PRT
<213> Homo sapiens

<400> 256

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Val Arg Val Lys Ala Tyr Tyr Arg Gly Asp Ile Met Ile Thr His Phe
            20                  25                  30
Glu Pro Ser Ile Ser Phe Glu Gly Leu Cys Asn Glu Val Arg Asp Met
        35                  40                  45
Cys Ser Phe Asp Asn Glu Gln Leu Phe Thr Met Lys Trp Ile Asp Glu
    50                  55                  60
Glu Gly Asp Pro Cys Thr Val Ser Ser Gln Leu Glu Leu Glu Glu Ala
65                  70                  75                  80
Phe Arg Leu Tyr Glu Leu Asn Lys Asp Ser Glu Leu Leu Ile His Val
                85                  90                  95
Phe Pro Cys Val Pro Glu Arg Pro Gly Met Pro Cys Pro Gly Glu Asp
            100                 105                 110
Lys Ser Ile Tyr Arg Arg Gly Ala Arg Arg Trp Arg Lys Leu Tyr Cys
        115                 120                 125
Ala Asn Gly His Thr Phe Gln Ala Lys Arg Phe Asn Arg Arg Ala His
    130                 135                 140
Cys Ala Ile Cys Thr Asp Arg Ile Trp Gly Leu Gly Arg Gln Gly Tyr
145                 150                 155                 160
Lys Cys Ile Asn Cys Lys Leu Leu Val His Lys Lys Cys His Lys Leu
                165                 170                 175
Val Thr Ile Glu Cys Gly Arg His Ser Leu Pro Gln Glu Pro Val Met
            180                 185                 190
Pro Met Asp Gln Ser Ser Met His Ser Asp His Ala Gln Thr Val Ile
        195                 200                 205
Pro Tyr Asn Pro Ser Ser His Glu Ser Leu Asp Gln Val Gly Glu Glu
    210                 215                 220
Lys Glu Ala Met Asn Thr Arg Glu Ser Gly Lys Ala Ser Ser Ser Leu
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Phe Leu Val Gly Leu His Ser Cys Phe Gln Thr Glu Ser Arg Leu Phe
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<213> Homo sapiens

<400> 257

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<213> Homo sapiens

<400> 258

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Arg Lys Phe Lys Met Ala Ala Ala Glu Thr Gln Ser Leu Arg Glu Gln
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Pro Glu Met Glu Asp Ala Asn Ser Glu Lys Ser Ile Asn Glu Glu Asn
    50                  55                  60
Gly Glu Val Ser Glu Asp Gln Ser Gln Asn Lys His Ser Arg His Lys
65                  70                  75                  80
Lys Lys Lys His Lys His Arg Ser Lys His Lys Lys His Lys His Ser
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Leu Glu Lys Gln Arg Ala Leu Ile Lys Ala Glu Leu Asp Asn Glu Leu
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Glu Ser Gly Ser Glu Glu Glu Gly Glu Ile His Glu Lys Ala Arg Asn
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Lys Ser Lys Asp Arg Arg Ser Arg Ser Lys Glu Arg Lys Ser Lys Arg
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Arg Ser Arg Ser Pro Leu Leu Asn Asp Arg Arg Ser Lys Gln Ser Lys
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Pro Arg Arg Arg Ser Arg Ser Pro Arg Arg Arg Asp Arg Gly Arg Arg
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Ser Glu Gly Met Lys Val Glu Gln Glu Ser Ser Ser Asp Asp Asn Leu
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Gly Ile Gly Lys Asp Phe Lys Glu Asn Pro Asn Leu Arg Asp Asn Trp
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Lys Arg Tyr Asn Val Tyr Gly Tyr Thr Gly Gln Gly Val Phe Ser Asn
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Val Val Arg Ala Arg Asp Asn Ala Arg Ala Asn Gln Glu Val Ala Val
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Lys Ile Ile Arg Asn Asn Glu Leu Met Gln Lys Thr Gly Leu Lys Glu
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Leu Glu Phe Leu Lys Lys Leu Asn Asp Ala Asp Pro Asp Asp Lys Phe
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His Cys Leu Arg Leu Phe Arg His Phe Tyr His Lys Gln His Leu Cys
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Tyr Gly Lys Asp Val Gly Leu His Ile Lys Ala Val Arg Ser Tyr Ser
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Gln Gln Leu Phe Leu Ala Leu Lys Leu Leu Lys Arg Cys Asn Ile Leu
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Cys Thr Leu Tyr Glu Leu Tyr Thr Gly Lys Ile Leu Phe Pro Gly Lys
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Thr Asn Asn His Met Leu Lys Leu Ala Met Asp Leu Lys Gly Lys Met
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Pro Asn Lys Met Ile Arg Lys Gly Val Phe Lys Asp Gln His Phe Asp
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Gln Asn Leu Asn Phe Met Tyr Ile Glu Val Asp Lys Val Thr Glu Arg
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Glu Lys Val Thr Val Met Ser Thr Ile Asn Pro Thr Lys Asp Leu Leu
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Pro Pro Leu Pro Val Leu Leu Ala Asp Pro Gly Ala Pro Thr Pro Val
20 25 30
Asn Pro Cys Cys Tyr Tyr Pro Cys Gln His Gln Gly Ile Cys Val Arg
35 40 45
Phe Gly Leu Asp Arg Tyr Gln Cys Asp Cys Thr Arg Thr Gly Tyr Ser
50 55 60

Gly Pro Asn Cys Thr Ile Pro Gly Leu Trp Thr Trp Leu Arg Asn Ser
65 70 75 80
Leu Arg Pro Ser Pro Ser Phe Thr His Phe Leu Leu Thr His Gly Arg
85 90 95
Trp Phe Trp Glu Phe Val Asn Ala Thr Phe Ile Arg Glu Met Leu Met
100 105 110
Arg Leu Val Leu Thr Val Arg Ser Asn Leu Ile Pro Ser Pro Pro Thr
115 120 125
Tyr Asn Ser Ala His Asp Tyr Ile Ser Trp Glu Ser Phe Ser Asn Val
130 135 140
Ser Tyr Tyr Thr Arg Ile Leu Pro Ser Val Pro Lys Asp Cys Pro Thr
145 150 155 160
Pro Met Gly Thr Lys Gly Lys Lys Gln Leu Pro Asp Ala Gln Leu Leu
165 170 175
Ala Arg Arg Phe Leu Leu Arg Arg Lys Phe Ile Pro Asp Pro Gln Gly
180 185 190
Thr Asn Leu Met Phe Ala Phe Phe Ala Gln His Phe Thr His Gln Phe
195 200 205
Phe Lys Thr Ser Gly Lys Met Gly Pro Gly Phe Thr Lys Ala Leu Gly
210 215 220
His Gly Val Asp Leu Gly His Ile Tyr Gly Asp Asn Leu Glu Arg Gln
225 230 235 240
Tyr Gln Leu Arg Leu Phe Lys Asp Gly Lys Leu Lys Tyr Gln Val Leu
245 250 255
Asp Gly Glu Met Tyr Pro Pro Ser Val Glu Glu Ala Pro Val Leu Met
260 265 270
His Tyr Pro Arg Gly Ile Pro Pro Gln Ser Gln Met Ala Val Gly Gln
275 280 285
Glu Val Phe Gly Leu Leu Pro Gly Leu Met Leu Tyr Ala Thr Leu Trp
290 295 300
Leu Arg Glu His Asn Arg Val Cys Asp Leu Leu Lys Ala Glu His Pro
305 310 315 320
Thr Trp Gly Asp Glu Gln Leu Phe Gln Thr Thr Arg Leu Ile Leu Ile
325 330 335
Gly Glu Thr Ile Lys Ile Val Ile Glu Glu Tyr Val Gln Gln Leu Ser
340 345 350
Gly Tyr Phe Leu Gln Leu Lys Phe Asp Pro Glu Leu Leu Phe Gly Val
355 360 365
Gln Phe Gln Tyr Arg Asn Arg Ile Ala Met Glu Phe Asn His Leu Tyr
370 375 380
His Trp His Pro Leu Met Pro Asp Ser Phe Lys Val Gly Ser Gln Glu
385 390 395 400
Tyr Ser Tyr Glu Gln Phe Leu Phe Asn Thr Ser Met Leu Val Asp Tyr
405 410 415
Gly Val Glu Ala Leu Val Asp Ala Phe Ser Arg Gln Ile Ala Gly Arg
420 425 430
Ile Gly Gly Gly Arg Asn Met Asp His His Ile Leu His Val Ala Val
435 440 445
Asp Val Ile Arg Glu Ser Arg Glu Met Arg Leu Gln Pro Phe Asn Glu
450 455 460
Tyr Arg Lys Arg Phe Gly Met Lys Pro Tyr Thr Ser Phe Gln Glu Leu
465 470 475 480
Val Gly Glu Lys Glu Met Ala Ala Glu Leu Glu Glu Leu Tyr Gly Asp
485 490 495
Ile Asp Ala Leu Glu Phe Tyr Pro Gly Leu Leu Leu Glu Lys Cys His
500 505 510
Pro Asn Ser Ile Phe Gly Glu Ser Met Ile Glu Ile Gly Ala Pro Phe
515 520 525

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Ser Leu Lys Gly Leu Leu Gly Asn Pro Ile Cys Ser Pro Glu Tyr Trp
    530                 535                 540
Lys Pro Ser Thr Phe Gly Gly Glu Val Gly Phe Asn Ile Val Lys Thr
545                 550                 555                 560
Ala Thr Leu Lys Lys Leu Val Cys Leu Asn Thr Lys Thr Cys Pro Tyr
                565                 570                 575
Val Ser Phe Arg Val Pro Asp Ala Ser Gln Asp Asp Gly Pro Ala Val
            580                 585                 590
Glu Arg Pro Ser Thr Glu Leu
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<210> 265
<211> 3000
<212> DNA
<213> Homo sapiens

<400> 265
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agaaatggaa agtacagact tctgaaaata tctattgaaa atgagcaact tgtgattgga 180
tcatatagtc agccttcaga ttcctgggat aaggattatg attcctttgt tttacccctg 240
ttggaggaca aacaaccatg ctatatatta ttcaggttag attctcagaa tgcccaggga 300
tatgaatgga tattcattgc atggtctcca gatcattctc atgttcgtca aaaaatgttg 360
tatgcagcaa caagagcaac tctgaagaag gaatttggag gtggccacat taaagatgaa 420
gtatttggaa cagtaaagga agatgtatca ttacatggat ataaaaaata cttgctgtca 480
caatcttccc ctgcccccact gactgcagct gaggaagaac tacgacagat taaaatcaat 540
gaggtacaga ctgacgtggg tgtggacact aagcatcaaa cactacaagg agtagcattt 600
cccatttctc gagaagcctt tcaggctttg gaaaaattga ataatagaca gctcaactat 660
gtgcagttgg aaatagatat aaaaaatgaa attataattt tggccaacac aacaaataca 720
gaactgaaag atttgccaaa gaggattccc aaggattcag ctcgttacca tttctttctg 780
tataaacatt cccatgaagg agactattta gagtccatag tttttattta ttcaatgcct 840
ggatacacat gcagtataag agagcggatg ctgtattcta gctgcaagag ccgtctgcta 900
gaaattgtag aaagacaact acaaatggat gtaattagaa agatcgagat agacaatggg 960
gatgagttga ctgcagactt cctttatgaa gaagtacatc ccaagcagca tgcacacaag 1020
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ggcccagcgg aaactgaagc tactactgat taaagtcatc acattaaaca ttgtaatact 1140
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agtagggaaa aaaattgtac tttttggaaa atagcacttt tcacttctgt gtgtttttaa 1260
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actactttct tgtgggacag aaagacctta aaatattcat attacttaat gaatatgtta 1500
aggaccaggc tagagtattt tctaagctgg aaacttagtg tgccttggaa aagccgcaag 1560
ttgcttactc cgagtagctg tgctagctct gtcagactgt aggatcatgt ctgcaacttt 1620
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atttctgatg acattgaaag actttaaaca gccttagtaa attatctttc taatgctctg 1800
tgaggccaaa catttatgtt cagattgaaa tttaaattaa tatcattcaa aaggaaacaa 1860
aaaatgttga gttttaaaaa tcaggattga ctttttctc caaaaccata catttatggg 1920
caaattgtgt tctttatcac ttccgagcaa atactcagat ttaaaattac tttaaagtcc 1980
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gagcctcata tttctttgat acttgaaata gagggagcta gaacacttaa tgtttaatct 2160
gttaaacctg ctgcaagagc cataactttg aggcattttc taaatgaact gtggggatcc 2220
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atttcatagt gtgaagcact catttctaaa ccttattatc taaggtaata tatgcacctt 2340
tcagaaattt gtgttcgagt aagtaaagca tattagaata attgtgggtt gacagatttt 2400
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taaaatagaa tttagagtat ttggggtttt gtttgtttac aaataatcag actataatat 2460
ttaaacatgc aaaataactg acaataatgt tgcacttgtt tactaaagat ataagttgtt 2520
ccatgggtgt acacgtagac agacacacat acacccaaat tattgcatta agaatcctgg 2580
agcagaccat agctgaagct gttattttca gtcaggaaga ctacctgtca tgaaggtata 2640
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actacactac attaaagtaa atggacattc cagaatatag atgtgattat agtcttaaac 2760
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tcatcgttta cagtatgttt tagttggcag tatcatacct agatggtgaa taacatattc 2880
ccagtaaatt tatatagcag tgaagaatta catgccttct ggtggacatt ttataagtgc 2940
attttatatc acaataaaaa ttttttctct ttaaaaaaaa aaaacaagaa aaaaaaaaaa 3000

<210> 266
<211> 350
<212> PRT
<213> Homo sapiens

<400> 266
Met Ser His Gln Thr Gly Ile Gln Ala Ser Glu Asp Val Lys Glu Ile
1   5   10   15
Phe Ala Arg Ala Arg Asn Gly Lys Tyr Arg Leu Leu Lys Ile Ser Ile
            20   25   30
Glu Asn Glu Gln Leu Val Ile Gly Ser Tyr Ser Gln Pro Ser Asp Ser
        35   40   45
Trp Asp Lys Asp Tyr Asp Ser Phe Val Leu Pro Leu Leu Glu Asp Lys
    50   55   60
Gln Pro Cys Tyr Ile Leu Phe Arg Leu Asp Ser Gln Asn Ala Gln Gly
65   70   75   80
Tyr Glu Trp Ile Phe Ile Ala Trp Ser Pro Asp His Ser His Val Arg
                85   90   95
Gln Lys Met Leu Tyr Ala Ala Thr Arg Ala Thr Leu Lys Lys Glu Phe
            100   105   110
Gly Gly Gly His Ile Lys Asp Glu Val Phe Gly Thr Val Lys Glu Asp
        115   120   125
Val Ser Leu His Gly Tyr Lys Lys Tyr Leu Leu Ser Gln Ser Ser Pro
    130   135   140
Ala Pro Leu Thr Ala Ala Glu Glu Glu Leu Arg Gln Ile Lys Ile Asn
145   150   155   160
Glu Val Gln Thr Asp Val Gly Val Asp Thr Lys His Gln Thr Leu Gln
                165   170   175
Gly Val Ala Phe Pro Ile Ser Arg Glu Ala Phe Gln Ala Leu Glu Lys
            180   185   190
Leu Asn Asn Arg Gln Leu Asn Tyr Val Gln Leu Glu Ile Asp Ile Lys
        195   200   205
Asn Glu Ile Ile Ile Leu Ala Asn Thr Thr Asn Thr Glu Leu Lys Asp
    210   215   220
Leu Pro Lys Arg Ile Pro Lys Asp Ser Ala Arg Tyr His Phe Phe Leu
225   230   235   240
Tyr Lys His Ser His Glu Gly Asp Tyr Leu Glu Ser Ile Val Phe Ile
                245   250   255
Tyr Ser Met Pro Gly Tyr Thr Cys Ser Ile Arg Glu Arg Met Leu Tyr
            260   265   270
Ser Ser Cys Lys Ser Arg Leu Leu Glu Ile Val Glu Arg Gln Leu Gln
        275   280   285
Met Asp Val Ile Arg Lys Ile Glu Ile Asp Asn Gly Asp Glu Leu Thr
    290   295   300
Ala Asp Phe Leu Tyr Glu Glu Val His Pro Lys Gln His Ala His Lys
305   310   315   320

Gln Ser Phe Ala Lys Pro Lys Gly Pro Ala Gly Lys Arg Gly Ile Arg
325 330 335
Arg Leu Ile Arg Gly Pro Ala Glu Thr Glu Ala Thr Thr Asp
340 345 350

<210> 267
<211> 358
<212> DNA
<213> Homo sapiens

<400> 267
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tgtgcgcgac gggctcagaa tgtagcccca tgggcgggac tcgaggctcg gtggacggcc 120
ttgcaggagg tacccggaac tccacgagtg acctcgcgat ctggcccggc tcccgttcgt 180
cgcaacagcg tgactacagg gtatggcggg gtccgggcac tgtgcggctg gacccccagt 240
tctggggcca cgccgcggaa ccgcttactg ctgcagcttt tggggtcgcc cggccgccgc 300
tattacagtc ttccccgca tcagaaggtt ccattgcctt ctctttcccc cacaatgc 358

<210> 268
<211> 103
<212> PRT
<213> Homo sapiens

<400> 268
Met Trp Arg Val Cys Ala Arg Arg Ala Gln Asn Val Ala Pro Trp Ala
1 5 10 15
Gly Leu Glu Ala Arg Trp Thr Ala Leu Gln Glu Val Pro Gly Thr Pro
20 25 30
Arg Val Thr Ser Arg Ser Gly Pro Ala Pro Val Arg Arg Asn Ser Val
35 40 45
Thr Thr Gly Tyr Gly Gly Val Arg Ala Leu Cys Gly Trp Thr Pro Ser
50 55 60
Ser Gly Ala Thr Pro Arg Asn Arg Leu Leu Leu Gln Leu Leu Gly Ser
65 70 75 80
Pro Gly Arg Arg Tyr Tyr Ser Leu Pro Pro His Gln Lys Val Pro Leu
85 90 95
Pro Ser Leu Ser Pro Thr Met
100

<210> 269
<211> 607
<212> DNA
<213> Homo sapiens

<400> 269
ggactgttga agacaggtct ccacacacag ctccagcagc cacatttgca accttggcca 60
tctgtccaga acctgctccc acctcaggcc caggcpaacc gtgcactgct gcaatgggct 120
ctgagctgga gacggcgatg gagaccctca tcaacgtgtt ccacgcccac tcgggcaaag 180
aggggggacaa gtacaagctg agcaagaagg agctgaaaga gctgctgcag acggagctct 240
ctggcttcct ggatgcccag aaggatgtgg atgctgtgga caaggtgatg aaggagctag 300
acgagaatgg agacggggag gtggacttcc aggagtatgt ggtgcttgtg gctgctctca 360
cagtggcctg taacaatttc ttctgggaga acagttgagc agacagccac attgggcagc 420
gcccttcctc tccaccctcc cagacctgcc tcttccccct gcttccacct caccccactt 480
atccctctcc ataaccccac ccttgcccac cccaccccca cccccaccaa gggcgcaaga 540
gtagcggtcc aagcctgcaa ctcatctttc attaaaggct tctctctcac cagcaaaaaa 600
aaaaaaa 607

<210> 270
<211> 94
<212> PRT
<213> Homo sapiens

<400> 270
Met Gly Ser Glu Leu Glu Thr Ala Met Glu Thr Leu Ile Asn Val Phe
1   5   10   15
His Ala His Ser Gly Lys Glu Gly Asp Lys Tyr Lys Leu Ser Lys Lys
            20   25   30
Glu Leu Lys Glu Leu Leu Gln Thr Glu Leu Ser Gly Phe Leu Asp Ala
        35   40   45
Gln Lys Asp Val Asp Ala Val Asp Lys Val Met Lys Glu Leu Asp Glu
    50   55   60
Asn Gly Asp Gly Glu Val Asp Phe Gln Glu Tyr Val Val Leu Val Ala
65   70   75   80
Ala Leu Thr Val Ala Cys Asn Asn Phe Phe Trp Glu Asn Ser
                85   90

<210> 271
<211> 595
<212> DNA
<213> Homo sapiens

<400> 271
gggcaaggct gggccgggaa gggcgtgggt tgaggagagg ctccagaccc gcacgccgcg 60
cgcacagagc tctcagcgcc gctcccagcc acagcctccc gcgcctcgct cagctccaac 120
atggcaaaaa tctccagccc tacagagact gagcggtgca tcgagtccct gattgctgtc 180
ttccagaagt atgctggaaa ggatggttat aactacactc tctccaagac agagttccta 240
agcttcatga atacagaact agctgccttc acaaagaacc agaaggaccc tggtgtcctt 300
gaccgcatga tgaagaaact ggacaccaac agtgatggtc agctagattt ctcagaattt 360
cttaatctga ttggtggcct agctatggct tgccatgact ccttcctcaa ggctgtccct 420
tcccagaagc ggacctgagg accccttggc cctggccttc aaacccaccc cctttccttc 480
cagcctttct gtcatcatct ccacagccca cccatcccct gagcacacta accacctcat 540
gcaggcccca cctgccaata gtaataaagc aatgtcactt ttttaaaaca tgaaa 595

<210> 272
<211> 105
<212> PRT
<213> Homo sapiens

<400> 272
Met Ala Lys Ile Ser Ser Pro Thr Glu Thr Glu Arg Cys Ile Glu Ser
1   5   10   15
Leu Ile Ala Val Phe Gln Lys Tyr Ala Gly Lys Asp Gly Tyr Asn Tyr
            20   25   30
Thr Leu Ser Lys Thr Glu Phe Leu Ser Phe Met Asn Thr Glu Leu Ala
        35   40   45
Ala Phe Thr Lys Asn Gln Lys Asp Pro Gly Val Leu Asp Arg Met Met
    50   55   60
Lys Lys Leu Asp Thr Asn Ser Asp Gly Gln Leu Asp Phe Ser Glu Phe
65   70   75   80
Leu Asn Leu Ile Gly Gly Leu Ala Met Ala Cys His Asp Ser Phe Leu
                85   90   95
Lys Ala Val Pro Ser Gln Lys Arg Thr
            100   105

<210> 273
<211> 428
<212> DNA
<213> Homo sapiens

<400> 273
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ggcgctggct gtgctggtca ctaccttcca caagtactcc tgccaagagg gcgacaagtt 120
caagctgagt aagggggaaa tgaaggaact tctgcacaag gagctgccca gctttgtggg 180
ggagaaagtg gatgaggagg ggctgaagaa gctgatgggc agcctggatg agaacagtga 240
ccagcaggtg gacttccagg agtatgctgt tttcctggca ctcatcactg tcatgtgcaa 300
tgacttcttc cagggctgcc cagaccgacc ctgaagcaga actcttgact tcctgccatg 360
gatctcttgg gcccaggact gttgatgcct ttgagttttg tattcaataa actttttttg 420
tctgttga 428

<210> 274
<211> 97
<212> PRT
<213> Homo sapiens

<400> 274
Met Cys Ser Ser Leu Glu Gln Ala Leu Ala Val Leu Val Thr Thr Phe
1 5 10 15
His Lys Tyr Ser Cys Gln Glu Gly Asp Lys Phe Lys Leu Ser Lys Gly
20 25 30
Glu Met Lys Glu Leu Leu His Lys Glu Leu Pro Ser Phe Val Gly Glu
35 40 45
Lys Val Asp Glu Glu Gly Leu Lys Lys Leu Met Gly Ser Leu Asp Glu
50 55 60
Asn Ser Asp Gln Gln Val Asp Phe Gln Glu Tyr Ala Val Phe Leu Ala
65 70 75 80
Leu Ile Thr Val Met Cys Asn Asp Phe Phe Gln Gly Cys Pro Asp Arg
85 90 95
Pro

<210> 275
<211> 470
<212> DNA
<213> Homo sapiens

<400> 275
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catttggccg cctccctacc gctccaagcc cagccctcag ccatggcatg ccccctggat 120
caggccattg gcctcctcgt ggccatcttc cacaagtact ccggcaggga gggtgacaag 180
cacaccctga gcaagaagga gctgaaggag ctgatccaga aggagctcac cattggctcg 240
aagctgcagg atgctgaaat tgcaaggctg atggaagact tggaccggaa caaggaccag 300
gaggtgaact tccaggagta tgtcaccttc ctgggggcct tggctttgat ctacaatgaa 360
gccctcaagg gctgaaaata aatagggaag atggagacac ctctgggggt cctctctgag 420
tcaaatccag tggtgggtaa ttgtacaata aatttttttt ggtcaaattt 470

<210> 276
<211> 90
<212> PRT
<213> Homo sapiens

<400> 276
Met Ala Cys Pro Leu Asp Gln Ala Ile Gly Leu Leu Val Ala Ile Phe
1 5 10 15
His Lys Tyr Ser Gly Arg Glu Gly Asp Lys His Thr Leu Ser Lys Lys
20 25 30
Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu
35 40 45
Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys
50 55 60
Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu
65 70 75 80
Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly
85 90

<210> 277
<211> 3151
<212> DNA
<213> Homo sapiens

<400> 277
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gagcaggacc ctagacctct gcagcccata ccaggtctca tggaggggaa caagctggag 120
gagcaggact ctagccctcc acagtccact ccagggctca tgaaggggaa caagcgtgag 180
gagcaggggc tgggccccga acctgcggcg ccccagcagc ccacggcgga ggaggaggcc 240
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atccacggcg ccatccgcct ggtgtgctcc cagcacaacc gcatgaagac ggccttctgg 360
gcagtgctgt ggctctgcac ctttggcatg atgtactggc aattcggcct gcttttcgga 420
gagtacttca gctaccccgt cagcctcaac atcaacctca actcggacaa gctcgtcttc 480
cccgcagtga ccatctgcac cctcaatccc tacaggtacc cggaaattaa agaggagctg 540
gaggagctgg accgcatcac agagcagacg ctctttgacc tgtacaaata cagctccttc 600
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ttgcagcgcc tgagggtccc gcccccgcct cacggggccc gtcgagcccg tagcgtggcc 720
tccagcttgc gggacaacaa cccccaggtg gactggaagg actggaagat cggcttccag 780
ctgtgcaacc agaacaaatc ggactgcttc taccagacat actcatcagg ggtggatgcg 840
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ccatccctgg aggaggacac gctgggcaac ttcatcttcg cctgccgctt caaccaggtc 960
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cagccaggcc ctgctccctc tccagccttg acagcccctc cccctgccta tgccaccctg 2040
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gggccctgag agggaaggag aggtttctca caccaaggca gatgctcctc tggtgggagg 2160

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gtgctggccc tggcaagatt gaaggatgtg cagggcttcc tctcagagcc gcccaaactg 2220
ccgttgatgt gtggaggga agcaagatgg gtaagggctc aggaagttgc tccaagaaca 2280
gtagctgatg aagctgccca gaagtgcctt ggctccagcc ctgtacccct tggtactgcc 2340
tctgaacact ctggtttccc cacccaactg cggctaagtc tctttttccc ttggatcagc 2400
caagcgaaac ttggagcttt gacaaggaac tttcctaaga aaccgctgat aaccaggaca 2460
aaacacaacc aagggtacac gcaggcatgc acgggtttcc tgcccagcga cggcttaagc 2520
cagccccga ctggcctggc cacactgctc tccagtagca cagatgtctg ctcctcctct 2580
tgaacttggg tgggaaccc cacccaaaag cccccttgt tacttaggca attcccttc 2640
cctgactccc gagggctagg gctagagcag acccgggtaa gtaaaggcag acccagggct 2700
cctctagcct catacccgtg ccctcacaga gccatgcccc ggcacctctg ccctgtgtct 2760
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gcttctgcca catcttgtct tccccaaaat tgatcactcc gccttctcct gggctcccgt 2940
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tctcccttcc caactagact gtaagtgcct tgcggtcagg gactgaatct tgcccgttta 3060
tgtatgctcc atgtctagcc catcatcctg cttggagcaa gtaggcagga gctcaataaa 3120
tgtttgttgc atgaaaaaa aaaaaaaaa a                                3151
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<210> 278
<211> 669
<212> PRT
<213> Homo sapiens

<400> 278

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Met Glu Gly Asn Lys Leu Glu Glu Gln Asp Ser Ser Pro Pro Gln Ser
1               5                   10                  15
Thr Pro Gly Leu Met Lys Gly Asn Lys Arg Glu Glu Gln Gly Leu Gly
            20                  25                  30
Pro Glu Pro Ala Ala Pro Gln Gln Pro Thr Ala Glu Glu Glu Ala Leu
        35                  40                  45
Ile Glu Phe His Arg Ser Tyr Arg Glu Leu Phe Glu Phe Phe Cys Asn
    50                  55                  60
Asn Thr Thr Ile His Gly Ala Ile Arg Leu Val Cys Ser Gln His Asn
65                  70                  75                  80
Arg Met Lys Thr Ala Phe Trp Ala Val Leu Trp Leu Cys Thr Phe Gly
                85                  90                  95
Met Met Tyr Trp Gln Phe Gly Leu Leu Phe Gly Glu Tyr Phe Ser Tyr
            100                 105                 110
Pro Val Ser Leu Asn Ile Asn Leu Asn Ser Asp Lys Leu Val Phe Pro
        115                 120                 125
Ala Val Thr Ile Cys Thr Leu Asn Pro Tyr Arg Tyr Pro Glu Ile Lys
    130                 135                 140
Glu Glu Leu Glu Glu Leu Asp Arg Ile Thr Glu Gln Thr Leu Phe Asp
145                 150                 155                 160
Leu Tyr Lys Tyr Ser Ser Phe Thr Thr Leu Val Ala Gly Ser Arg Ser
                165                 170                 175
Arg Arg Asp Leu Arg Gly Thr Leu Pro His Pro Leu Gln Arg Leu Arg
            180                 185                 190
Val Pro Pro Pro Pro His Gly Ala Arg Arg Ala Arg Ser Val Ala Ser
        195                 200                 205
Ser Leu Arg Asp Asn Asn Pro Gln Val Asp Trp Lys Asp Trp Lys Ile
    210                 215                 220
Gly Phe Gln Leu Cys Asn Gln Asn Lys Ser Asp Cys Phe Tyr Gln Thr
225                 230                 235                 240
Tyr Ser Ser Gly Val Asp Ala Val Arg Glu Trp Tyr Arg Phe His Tyr
                245                 250                 255
Ile Asn Ile Leu Ser Arg Leu Pro Glu Thr Leu Pro Ser Leu Glu Glu
            260                 265                 270
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Asp Thr Leu Gly Asn Phe Ile Phe Ala Cys Arg Phe Asn Gln Val Ser
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Cys Asn Gln Ala Asn Tyr Ser His Phe His His Pro Met Tyr Gly Asn
    290                 295                 300
Cys Tyr Thr Phe Asn Asp Lys Asn Asn Ser Asn Leu Trp Met Ser Ser
305                 310                 315                 320
Met Pro Gly Ile Asn Asn Gly Leu Ser Leu Met Leu Arg Ala Glu Gln
                325                 330                 335
Asn Asp Phe Ile Pro Leu Leu Ser Thr Val Thr Gly Ala Arg Val Met
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Val His Gly Gln Asp Glu Pro Ala Phe Met Asp Asp Gly Gly Phe Asn
        355                 360                 365
Leu Arg Pro Gly Val Glu Thr Ser Ile Ser Met Arg Lys Glu Thr Leu
    370                 375                 380
Asp Arg Leu Gly Gly Asp Tyr Gly Asp Cys Thr Lys Asn Gly Ser Asp
385                 390                 395                 400
Val Pro Val Glu Asn Leu Tyr Pro Ser Lys Tyr Thr Gln Gln Val Cys
                405                 410                 415
Ile His Ser Cys Phe Gln Glu Ser Met Ile Lys Glu Cys Gly Cys Ala
            420                 425                 430
Tyr Ile Phe Tyr Pro Arg Pro Gln Asn Val Glu Tyr Cys Asp Tyr Arg
        435                 440                 445
Lys His Ser Ser Trp Gly Tyr Cys Tyr Tyr Lys Leu Gln Val Asp Phe
    450                 455                 460
Ser Ser Asp His Leu Gly Cys Phe Thr Lys Cys Arg Lys Pro Cys Ser
465                 470                 475                 480
Val Thr Ser Tyr Gln Leu Ser Ala Gly Tyr Ser Arg Trp Pro Ser Val
                485                 490                 495
Thr Ser Gln Glu Trp Val Phe Gln Met Leu Ser Arg Gln Asn Asn Tyr
            500                 505                 510
Thr Val Asn Asn Lys Arg Asn Gly Val Ala Lys Val Asn Ile Phe Phe
        515                 520                 525
Lys Glu Leu Asn Tyr Lys Thr Asn Ser Glu Ser Pro Ser Val Thr Met
    530                 535                 540
Val Thr Leu Leu Ser Asn Leu Gly Ser Gln Trp Ser Leu Trp Phe Gly
545                 550                 555                 560
Ser Ser Val Leu Ser Val Val Glu Met Ala Glu Leu Val Phe Asp Leu
                565                 570                 575
Leu Val Ile Met Phe Leu Met Leu Leu Arg Arg Phe Arg Ser Arg Tyr
            580                 585                 590
Trp Ser Pro Gly Arg Gly Gly Arg Gly Ala Gln Glu Val Ala Ser Thr
        595                 600                 605
Leu Ala Ser Ser Pro Pro Ser His Phe Cys Pro His Pro Met Ser Leu
    610                 615                 620
Ser Leu Ser Gln Pro Gly Pro Ala Pro Ser Pro Ala Leu Thr Ala Pro
625                 630                 635                 640
Pro Pro Ala Tyr Ala Thr Leu Gly Pro Arg Pro Ser Pro Gly Gly Ser
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Ala Gly Ala Ser Ser Ser Thr Cys Pro Leu Gly Gly Pro
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<210> 279
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<212> DNA
<213> Homo sapiens

<220>

<221> misc_feature
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<211> 669
<212> PRT
<213> Homo sapiens

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20 25 30
Pro Glu Pro Ala Ala Pro Gln Gln Pro Thr Ala Glu Glu Glu Ala Leu
35 40 45
Ile Glu Phe His Arg Ser Tyr Arg Glu Leu Phe Glu Phe Phe Cys Asn
50 55 60
Asn Thr Thr Ile His Gly Ala Ile Arg Leu Val Cys Ser Gln His Asn
65 70 75 80
Arg Met Lys Thr Ala Phe Trp Ala Val Leu Trp Leu Cys Thr Phe Gly
85 90 95
Met Met Tyr Trp Gln Phe Gly Leu Leu Phe Gly Glu Tyr Phe Ser Tyr
100 105 110
Pro Val Ser Leu Asn Ile Asn Leu Asn Ser Asp Lys Leu Val Phe Pro
115 120 125
Ala Val Thr Ile Cys Thr Leu Asn Pro Tyr Arg Tyr Pro Glu Ile Lys
130 135 140
Glu Glu Leu Glu Glu Leu Asp Arg Ile Thr Glu Gln Thr Leu Phe Asp
145 150 155 160
Leu Tyr Lys Tyr Ser Ser Phe Thr Thr Leu Val Ala Gly Ser Arg Ser
165 170 175
Arg Arg Asp Leu Arg Gly Thr Leu Pro His Pro Leu Gln Arg Leu Arg
180 185 190
Val Pro Pro Pro Pro His Gly Ala Arg Arg Ala Arg Ser Val Ala Ser
195 200 205
Ser Leu Arg Asp Asn Asn Pro Gln Val Asp Trp Lys Asp Trp Lys Ile
210 215 220
Gly Phe Gln Leu Cys Asn Gln Asn Lys Ser Asp Cys Phe Tyr Gln Thr
225 230 235 240
Tyr Ser Ser Gly Val Asp Ala Val Arg Glu Trp Tyr Arg Phe His Tyr
245 250 255
Ile Asn Ile Leu Ser Arg Leu Pro Glu Thr Leu Pro Ser Leu Glu Glu
260 265 270
Asp Thr Leu Gly Asn Phe Ile Phe Ala Cys Arg Phe Asn Gln Val Ser
275 280 285
Cys Asn Gln Ala Asn Tyr Ser His Phe His His Pro Met Tyr Gly Asn
290 295 300
Cys Tyr Thr Phe Asn Asp Lys Asn Asn Ser Asn Leu Trp Met Ser Ser
305 310 315 320
Met Pro Gly Ile Asn Asn Gly Leu Ser Leu Met Leu Arg Ala Glu Gln
325 330 335
Asn Asp Phe Ile Pro Leu Leu Ser Thr Val Thr Gly Ala Arg Val Met
340 345 350
Val His Gly Gln Asp Glu Pro Ala Phe Met Asp Asp Gly Gly Phe Asn
355 360 365
Leu Arg Pro Gly Val Glu Thr Ser Ile Ser Met Arg Lys Glu Thr Leu
370 375 380
Asp Arg Leu Gly Gly Asp Tyr Gly Asp Cys Thr Lys Asn Gly Ser Asp
385 390 395 400
Val Pro Val Glu Asn Leu Tyr Pro Ser Lys Tyr Thr Gln Gln Val Cys

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                405                 410                 415
Ile His Ser Cys Phe Gln Glu Ser Met Ile Lys Glu Cys Gly Cys Ala
            420                 425                 430
Tyr Ile Phe Tyr Pro Arg Pro Gln Asn Val Glu Tyr Cys Asp Tyr Arg
        435                 440                 445
Lys His Ser Ser Trp Gly Tyr Cys Tyr Tyr Lys Leu Gln Val Asp Phe
    450                 455                 460
Ser Ser Asp His Leu Gly Cys Phe Thr Lys Cys Arg Lys Pro Cys Ser
465                 470                 475                 480
Val Thr Ser Tyr Gln Leu Ser Ala Gly Tyr Ser Arg Trp Pro Ser Val
                485                 490                 495
Thr Ser Gln Glu Trp Val Phe Gln Met Leu Ser Arg Gln Asn Asn Tyr
            500                 505                 510
Thr Val Asn Asn Lys Arg Asn Gly Val Ala Lys Val Asn Ile Phe Phe
        515                 520                 525
Lys Glu Leu Asn Tyr Lys Thr Asn Ser Glu Ser Pro Ser Val Thr Met
    530                 535                 540
Val Thr Leu Leu Ser Asn Leu Gly Ser Gln Trp Ser Leu Trp Phe Gly
545                 550                 555                 560
Ser Ser Val Leu Ser Val Val Glu Met Ala Glu Leu Val Phe Asp Leu
                565                 570                 575
Leu Val Ile Met Phe Leu Met Leu Leu Arg Arg Phe Arg Ser Arg Tyr
            580                 585                 590
Trp Ser Pro Gly Arg Gly Gly Arg Gly Ala Gln Glu Val Ala Ser Thr
        595                 600                 605
Leu Ala Ser Ser Pro Pro Ser His Phe Cys Pro His Pro Met Ser Leu
    610                 615                 620
Ser Leu Ser Gln Pro Gly Pro Ala Pro Ser Pro Ala Leu Thr Ala Pro
625                 630                 635                 640
Pro Pro Ala Tyr Ala Thr Leu Gly Pro Arg Pro Ser Pro Gly Gly Ser
                645                 650                 655
Ala Gly Ala Ser Ser Ser Ala Cys Pro Leu Gly Gly Pro
            660                 665
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<210> 281
<211> 2892
<212> DNA
<213> Homo sapiens

<400> 281

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ccgaaccccg ccgtgtcctt cccgccgccc cgggtcaccc tgcccgccgg ccccgacatc 180
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<210> 282
<211> 176
<212> PRT
<213> Homo sapiens

<400> 282
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            20                  25                  30
Arg Thr Tyr Ser Gly Ala Phe Val Cys Leu Glu Ile Leu Phe Gly Gly
        35                  40                  45
Leu Val Trp Ile Leu Val Ala Ser Ser Asn Val Pro Leu Pro Leu Leu
    50                  55                  60
Gln Gly Trp Val Met Phe Val Ser Val Thr Ala Phe Phe Phe Ser Leu
65                  70                  75                  80
Leu Phe Leu Gly Met Phe Leu Ser Gly Met Val Ala Gln Ile Asp Ala
                85                  90                  95
Asn Trp Asn Phe Leu Asp Phe Ala Tyr His Phe Thr Val Phe Val Phe
            100                 105                 110
Tyr Phe Gly Ala Phe Leu Leu Glu Ala Ala Ala Thr Ser Leu His Asp
        115                 120                 125
Leu His Cys Asn Thr Thr Ile Thr Gly Gln Pro Leu Leu Ser Asp Asn
    130                 135                 140
Gln Tyr Asn Ile Asn Val Ala Ala Ser Ile Phe Ala Phe Met Thr Thr
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145                 150                 155                 160
Ala Cys Tyr Gly Cys Ser Leu Gly Leu Ala Leu Arg Arg Trp Arg Pro
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<210> 283
<211> 2530
<212> DNA
<213> Homo sapiens

<400> 283
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<210> 284
<211> 771
<212> PRT
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<213> Homo sapiens

<400> 284
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            20                  25                  30
Lys Leu Ser Tyr Lys Glu Met Leu Glu Ser Asn Asn Val Ile Thr Phe
        35                  40                  45
Asn Gly Leu Ala Asn Ser Ser Ser Tyr His Thr Phe Leu Leu Asp Glu
    50                  55                  60
Glu Arg Ser Arg Leu Tyr Val Gly Ala Lys Asp His Ile Phe Ser Phe
65                  70                  75                  80
Asp Leu Val Asn Ile Lys Asp Phe Gln Lys Ile Val Trp Pro Val Ser
                85                  90                  95
Tyr Thr Arg Arg Asp Glu Cys Lys Trp Ala Gly Lys Asp Ile Leu Lys
            100                 105                 110
Glu Cys Ala Asn Phe Ile Lys Val Leu Lys Ala Tyr Asn Gln Thr His
        115                 120                 125
Leu Tyr Ala Cys Gly Thr Gly Ala Phe His Pro Ile Cys Thr Tyr Ile
    130                 135                 140
Glu Ile Gly His His Pro Glu Asp Asn Ile Phe Lys Leu Glu Asn Ser
145                 150                 155                 160
His Phe Glu Asn Gly Arg Gly Lys Ser Pro Tyr Asp Pro Lys Leu Leu
                165                 170                 175
Thr Ala Ser Leu Leu Ile Asp Gly Glu Leu Tyr Ser Gly Thr Ala Ala
            180                 185                 190
Asp Phe Met Gly Arg Asp Phe Ala Ile Phe Arg Thr Leu Gly His His
        195                 200                 205
His Pro Ile Arg Thr Glu Gln His Asp Ser Arg Trp Leu Asn Asp Pro
    210                 215                 220
Lys Phe Ile Ser Ala His Leu Ile Ser Glu Ser Asp Asn Pro Glu Asp
225                 230                 235                 240
Asp Lys Val Tyr Phe Phe Phe Arg Glu Asn Ala Ile Asp Gly Glu His
                245                 250                 255
Ser Gly Lys Ala Thr His Ala Arg Ile Gly Gln Ile Cys Lys Asn Asp
            260                 265                 270
Phe Gly Gly His Arg Ser Leu Val Asn Lys Trp Thr Thr Phe Leu Lys
        275                 280                 285
Ala Arg Leu Ile Cys Ser Val Pro Gly Pro Asn Gly Ile Asp Thr His
    290                 295                 300
Phe Asp Glu Leu Gln Asp Val Phe Leu Met Asn Phe Lys Asp Pro Lys
305                 310                 315                 320
Asn Pro Val Val Tyr Gly Val Phe Thr Thr Ser Ser Asn Ile Phe Lys
                325                 330                 335
Gly Ser Ala Val Cys Met Tyr Ser Met Ser Asp Val Arg Arg Val Phe
            340                 345                 350
Leu Gly Pro Tyr Ala His Arg Asp Gly Pro Asn Tyr Gln Trp Val Pro
        355                 360                 365
Tyr Gln Gly Arg Val Pro Tyr Pro Arg Pro Gly Thr Cys Pro Ser Lys
    370                 375                 380
Thr Phe Gly Gly Phe Asp Ser Thr Lys Asp Leu Pro Asp Asp Val Ile
385                 390                 395                 400
Thr Phe Ala Arg Ser His Pro Ala Met Tyr Asn Pro Val Phe Pro Met
                405                 410                 415
Asn Asn Arg Pro Ile Val Ile Lys Thr Asp Val Asn Tyr Gln Phe Thr
            420                 425                 430
Gln Ile Val Val Asp Arg Val Asp Ala Glu Asp Gly Gln Tyr Asp Val
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        435                 440                 445
Met Phe Ile Gly Thr Asp Val Gly Thr Val Leu Lys Val Val Ser Ile
    450                 455                 460
Pro Lys Glu Thr Trp Tyr Asp Leu Glu Glu Val Leu Leu Glu Glu Met
465                 470                 475                 480
Thr Val Phe Arg Glu Pro Thr Ala Ile Ser Ala Met Glu Leu Ser Thr
                485                 490                 495
Lys Gln Gln Gln Leu Tyr Ile Gly Ser Thr Ala Gly Val Ala Gln Leu
            500                 505                 510
Pro Leu His Arg Cys Asp Ile Tyr Gly Lys Ala Cys Ala Glu Cys Cys
        515                 520                 525
Leu Ala Arg Asp Pro Tyr Cys Ala Trp Asp Gly Ser Ala Cys Ser Arg
    530                 535                 540
Tyr Phe Pro Thr Ala Lys Arg Arg Thr Arg Arg Gln Asp Ile Arg Asn
545                 550                 555                 560
Gly Asp Pro Leu Thr His Cys Ser Asp Leu His His Asp Asn His His
                565                 570                 575
Gly His Ser Pro Glu Glu Arg Ile Ile Tyr Gly Val Glu Asn Ser Ser
            580                 585                 590
Thr Phe Leu Glu Cys Ser Pro Lys Ser Gln Arg Ala Leu Val Tyr Trp
        595                 600                 605
Gln Phe Gln Arg Arg Asn Glu Glu Arg Lys Glu Glu Ile Arg Val Asp
    610                 615                 620
Asp His Ile Ile Arg Thr Asp Gln Gly Leu Leu Leu Arg Ser Leu Gln
625                 630                 635                 640
Gln Lys Asp Ser Gly Asn Tyr Leu Cys His Ala Val Glu His Gly Phe
                645                 650                 655
Ile Gln Thr Leu Leu Lys Val Thr Leu Glu Val Ile Asp Thr Glu His
            660                 665                 670
Leu Glu Glu Leu Leu His Lys Asp Asp Asp Gly Asp Gly Ser Lys Thr
        675                 680                 685
Lys Glu Met Ser Asn Ser Met Thr Pro Ser Gln Lys Val Trp Tyr Arg
    690                 695                 700
Asp Phe Met Gln Leu Ile Asn His Pro Asn Leu Asn Thr Met Asp Glu
705                 710                 715                 720
Phe Cys Glu Gln Val Trp Lys Arg Asp Arg Lys Gln Arg Arg Gln Arg
                725                 730                 735
Pro Gly His Thr Pro Gly Asn Ser Asn Lys Trp Lys His Leu Gln Glu
            740                 745                 750
Asn Lys Lys Gly Arg Asn Arg Arg Thr His Glu Phe Glu Arg Ala Pro
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Arg Ser Val
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<210> 285
<211> 3041
<212> DNA
<213> Homo sapiens

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agatgctgcc cagaagacag atacatccca ccatgatcag gatcacccaa ccttcaacaa 180
gatcaccccc aacctggctg agttcgcctt cagcctatac cgccagctgg cacaccagtc 240
caacagcacc aatatcttct tctccccagt gagcatcgct acagcctttg caatgctctc 300
cctggggacc aaggctgaca ctcacgatga aatcctggag ggcctgaatt tcaacctcac 360
ggagattccg gaggctcaga tccatgaagg cttccaggaa ctcctccgta ccctcaacca 420
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caacttcggg gacaccgaag aggccaagaa acagatcaac gattacgtgg agaagggtac 600
tcaagggaaa attgtggatt tggtcaagga gcttgacaga gacacagttt ttgctctggt 660
gaattacatc ttctttaaag gcaaatggga gagacccttt gaagtcaagg acaccgagga 720
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catgtttaac atccagcact gtaagaagct gtccagctgg gtgctgctga tgaaatacct 840
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agccccagtc attgctagta agacctgcct ttgagttggt atgatgttca agttagataa 2940
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 3041

<210> 286
<211> 418
<212> PRT
<213> Homo sapiens

<400> 286
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Cys Leu Val Pro Val Ser Leu Ala Glu Asp Pro Gln Gly Asp Ala Ala
20 25 30
Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
35 40 45
Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln

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    50                  55                  60
Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser
65                  70                  75                  80
Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr
                85                  90                  95
His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro
            100                 105                 110
Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn
        115                 120                 125
Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu
    130                 135                 140
Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys
145                 150                 155                 160
Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu
                165                 170                 175
Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys
            180                 185                 190
Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu
        195                 200                 205
Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
    210                 215                 220
Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val
225                 230                 235                 240
Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys
                245                 250                 255
Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala
            260                 265                 270
Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu
        275                 280                 285
Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp
    290                 295                 300
Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr
305                 310                 315                 320
Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
                325                 330                 335
Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys
            340                 345                 350
Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly
        355                 360                 365
Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile
    370                 375                 380
Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu
385                 390                 395                 400
Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
                405                 410                 415
Gln Lys
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<210> 287
<211> 3928
<212> DNA
<213> Homo sapiens

<220>
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<223> n = A,T,C or G

<400> 287
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gaggcttgtg gaggaaagga accaagtgac tctgatgttt acaaagcacc tatgaaaccc 1140
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aaaaaaaaan aaaaaaaaaa aaaaaaa 3928

<210> 288
<211> 293
<212> PRT
<213> Homo sapiens

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Cys Leu His Arg Thr Leu Thr Ser Trp Leu Arg Val Arg Phe Gly Thr
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Trp Asn Trp Ile Trp Arg Arg Cys Cys Arg Ala Ala Ser Ala Ala Val
35 40 45
Leu Ala Pro Leu Gly Phe Thr Leu Arg Lys Pro Pro Ala Val Gly Arg
50 55 60
Asn Arg Arg His His Arg His Pro Arg Gly Gly Ser Cys Leu Ala Ala
65 70 75 80
Ala His His Arg Met Arg Trp Arg Ala Asp Gly Arg Ser Leu Glu Lys
85 90 95
Leu Pro Val His Met Gly Leu Val Ile Thr Glu Val Glu Gln Glu Pro
100 105 110
Ser Phe Ser Asp Ile Ala Ser Leu Val Val Trp Cys Met Ala Val Gly
115 120 125
Ile Ser Tyr Ile Ser Val Tyr Asp His Gln Gly Ile Phe Lys Arg Asn
130 135 140
Asn Ser Arg Leu Met Asp Glu Ile Leu Lys Gln Gln Gln Glu Leu Leu
145 150 155 160
Gly Leu Asp Cys Ser Lys Tyr Ser Pro Glu Phe Ala Asn Ser Asn Asp
165 170 175
Lys Asp Asp Gln Val Leu Asn Cys His Leu Ala Val Lys Val Leu Ser
180 185 190
Pro Glu Asp Gly Lys Ala Asp Ile Val Arg Ala Ala Gln Asp Phe Cys
195 200 205
Gln Leu Val Ala Gln Lys Gln Lys Arg Pro Thr Asp Leu Asp Val Asp
210 215 220
Thr Leu Ala Ser Leu Leu Ser Ser Asn Gly Cys Pro Asp Pro Asp Leu
225 230 235 240
Val Leu Lys Phe Gly Pro Val Asp Ser Thr Leu Gly Phe Leu Pro Trp
245 250 255
His Ile Arg Leu Thr Glu Ile Val Ser Leu Pro Ser His Leu Asn Ile
260 265 270
Ser Tyr Glu Asp Phe Phe Ser Ala Leu Arg Gln Tyr Ala Ala Cys Glu
275 280 285
Gln Arg Leu Gly Lys
290

<210> 289

<211> 936
<212> DNA
<213> Homo sapiens

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gagaagaagc agagaaatat gctaaggaat ctctgaagga agaagatgaa tcagatgatg 780
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ctattaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa 936

<210> 290
<211> 248
<212> PRT
<213> Homo sapiens

<400> 290
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20 25 30
Asn Ser Ser Thr Ala Ile Gly Ile Arg Cys Lys Asp Gly Val Val Phe
35 40 45
Gly Val Glu Lys Leu Val Leu Ser Lys Leu Tyr Glu Glu Gly Ser Asn
50 55 60
Lys Arg Leu Phe Asn Val Asp Arg His Val Gly Met Ala Val Ala Gly
65 70 75 80
Leu Leu Ala Asp Ala Arg Ser Leu Ala Asp Ile Ala Arg Glu Glu Ala
85 90 95
Ser Asn Phe Arg Ser Asn Phe Gly Tyr Asn Ile Pro Leu Lys His Leu
100 105 110
Ala Asp Arg Val Ala Met Tyr Val His Ala Tyr Thr Leu Tyr Ser Ala
115 120 125
Val Arg Pro Phe Gly Cys Ser Val Asn Asp Gly Ala Gln Leu Tyr Met
130 135 140
Ile Asp Pro Ser Gly Val Ser Tyr Gly Tyr Trp Gly Cys Ala Ile Gly
145 150 155 160
Lys Ala Arg Gln Ala Ala Lys Thr Glu Ile Glu Lys Leu Gln Met Lys
165 170 175
Glu Met Thr Cys Arg Asp Ile Val Lys Glu Val Ala Lys Ile Ile Tyr
180 185 190
Ile Val His Asp Glu Val Lys Asp Lys Ala Phe Glu Leu Glu Leu Ser
195 200 205
Trp Val Gly Glu Leu Thr Asn Gly Arg His Glu Ile Val Pro Lys Asp
210 215 220
Ile Arg Glu Glu Ala Glu Lys Tyr Ala Lys Glu Ser Leu Lys Glu Glu
225 230 235 240

Asp Glu Ser Asp Asp Asp Asn Met
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<210> 291
<211> 2782
<212> DNA
<213> Homo sapiens

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<210> 292
<211> 461
<212> PRT
<213> Homo sapiens

<400> 292
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Met Arg Glu Thr Phe Arg Asn Leu Ala Ser Val Gly Lys Gln Trp Glu
        35                  40                  45
Asp Gln Asn Ile Glu Asp Pro Phe Lys Ile Pro Arg Arg Asn Ile Ser
    50                  55                  60
His Ile Pro Glu Arg Leu Cys Glu Ser Lys Glu Gly Gly Gln Gly Glu
65                  70                  75                  80
Glu Thr Phe Ser Gln Ile Pro Asp Gly Ile Leu Asn Lys Lys Thr Pro
                85                  90                  95
Gly Val Lys Pro Cys Glu Ser Ser Val Cys Gly Glu Val Gly Met Gly
            100                 105                 110
Pro Ser Ser Leu Asn Arg His Ile Arg Asp His Thr Gly Arg Glu Pro
        115                 120                 125
Asn Glu Tyr Gln Glu Tyr Gly Lys Lys Ser Tyr Thr Arg Asn Gln Cys
    130                 135                 140
Gly Arg Ala Leu Ser Tyr His Arg Ser Phe Pro Val Arg Glu Arg Thr
145                 150                 155                 160
His Pro Gly Gly Lys Pro Tyr Asp Cys Lys Glu Cys Gly Glu Thr Phe
                165                 170                 175
Ile Ser Leu Val Ser Ile Arg Arg His Met Leu Thr His Arg Gly Gly
            180                 185                 190
Val Pro Tyr Lys Cys Lys Val Cys Gly Lys Ala Phe Asp Tyr Pro Ser
        195                 200                 205
Leu Phe Arg Ile His Glu Arg Ser His Thr Gly Glu Lys Pro Tyr Glu
    210                 215                 220
Cys Lys Gln Cys Gly Lys Ala Phe Ser Cys Ser Ser Tyr Ile Arg Ile
225                 230                 235                 240
His Glu Arg Thr His Thr Gly Asp Lys Pro Tyr Glu Cys Lys Gln Cys
                245                 250                 255
Gly Lys Ala Phe Ser Cys Ser Lys Tyr Ile Arg Ile His Glu Arg Thr
            260                 265                 270
His Thr Gly Glu Lys Pro Tyr Glu Cys Lys Gln Cys Gly Lys Ala Phe
        275                 280                 285
Arg Cys Ala Ser Ser Val Arg Ser His Glu Arg Thr His Thr Gly Glu
    290                 295                 300
Lys Leu Phe Glu Cys Lys Glu Cys Gly Lys Ala Leu Thr Cys Leu Ala
305                 310                 315                 320
Ser Val Arg Arg His Met Ile Lys His Thr Gly Asn Gly Pro Tyr Lys
                325                 330                 335
Cys Lys Val Cys Gly Lys Ala Phe Asp Phe Pro Ser Ser Phe Arg Ile
            340                 345                 350
His Glu Arg Thr His Thr Gly Glu Lys Pro Tyr Asp Cys Lys Gln Cys
        355                 360                 365
Gly Lys Ala Phe Ser Cys Ser Ser Ser Phe Arg Lys His Glu Arg Ile
    370                 375                 380
His Thr Gly Glu Lys Pro Tyr Lys Cys Thr Lys Cys Gly Lys Ala Phe
385                 390                 395                 400
Ser Arg Ser Ser Tyr Phe Arg Ile His Glu Arg Thr His Thr Gly Glu
                405                 410                 415
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Lys Pro Tyr Glu Cys Lys Gln Cys Gly Lys Ala Phe Ser Arg Ser Thr
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Tyr Phe Arg Val His Glu Lys Ile His Thr Gly Glu Lys Pro Tyr Glu
435 440 445
Asn Pro Asn Pro Asn Ala Ser Val Val Pro Val Leu Ser
450 455 460

<210> 293
<211> 666
<212> DNA
<213> Homo sapiens

<400> 293
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aaaaaa 666

<210> 294
<211> 58
<212> PRT
<213> Homo sapiens

<400> 294
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Thr Leu Ala Pro Trp Ala Val Glu Gly Ser Gly Lys Cys Lys Leu Glu
20 25 30
Ser Leu Trp Ser Asn Leu Gly Cys Arg Val Arg Gly Gly Val Ser Leu
35 40 45
Trp Cys Gly Cys Val Pro Phe Cys Arg Leu
50 55

<210> 295
<211> 594
<212> DNA
<213> Homo sapiens

<400> 295
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<210> 296
<211> 132
<212> PRT
<213> Homo sapiens

<400> 296
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Thr Leu Ala Pro Trp Ala Val Glu Gly Ser Gly Lys Ser Phe Lys Ala
20 25 30
Gly Val Cys Pro Pro Lys Lys Ser Ala Gln Cys Leu Arg Tyr Lys Lys
35 40 45
Pro Glu Cys Gln Ser Asp Trp Gln Cys Pro Gly Lys Lys Arg Cys Cys
50 55 60
Pro Asp Thr Cys Gly Ile Lys Cys Leu Asp Pro Val Asp Thr Pro Asn
65 70 75 80
Pro Thr Arg Arg Lys Pro Gly Lys Cys Pro Val Thr Tyr Gly Gln Cys
85 90 95
Leu Met Leu Asn Pro Pro Asn Phe Cys Glu Met Asp Gly Gln Cys Lys
100 105 110
Arg Asp Leu Lys Cys Cys Met Gly Met Cys Gly Lys Ser Cys Val Ser
115 120 125
Pro Val Lys Ala
130

<210> 297
<211> 720
<212> DNA
<213> Homo sapiens

<400> 297
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<210> 298
<211> 127
<212> PRT
<213> Homo sapiens

<400> 298
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Thr Lys Glu Gly Val Met Tyr Val Gly Ala Lys Thr Lys Glu Asn Val
35 40 45
Val Gln Ser Val Thr Ser Val Ala Glu Lys Thr Lys Glu Gln Ala Asn
50 55 60
Ala Val Ser Glu Ala Val Val Ser Ser Val Asn Thr Val Ala Thr Lys
65 70 75 80
Thr Val Glu Glu Ala Glu Asn Ile Ala Val Thr Ser Gly Val Val Arg
85 90 95
Lys Glu Asp Leu Arg Pro Ser Ala Pro Gln Gln Glu Gly Val Ala Ser
100 105 110
Lys Glu Lys Glu Glu Val Ala Glu Glu Ala Gln Ser Gly Gly Asp
115 120 125

<210> 299
<211> 6981
<212> DNA
<213> Homo sapiens

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ccacgtcctt tcttgacctc tatcgcaacc cgaagagctt gactacttca ctccacaaca 5880
agacggtcat tgtcagtaag gatgagcagt atttgtttct ggtccgtgta gtggtaccct 5940
accaggggcc atcctctgac tacgttgtag tgaagatgat cccggacagc aggcttccac 6000
cccgtcacct gcatgtggtt catacgggca aaacctccgt ggtcatcaag tgggaatcac 6060
cgtatgactc tcctgaccag gacttgttgt atgcaattgc agtcaaagat ctcataagaa 6120
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agttggagcc tggcggaaaa taccacatca ttgtccaact ggggaacatg agcaaagatt 6240
ccagcataaa aattaccaca gtttcattat cagcacctga tgccttaaaa atcataacag 6300
aaaatgatca tgttcttctg ttttggaaaa gcctggcttt aaaggaaaag cattttaatg 6360
aaagcagggg ctatgagata cacatgtttg atagtgccat gaatatcaca gcttaccttg 6420
ggaatactac tgacaatttc tttaaaattt ccaacctgaa gatgggtcat aattacacgt 6480
tcaccgtcca agcaagatgc ctttttggca accagatctg tggggagcct gccatcctgc 6540
tgtacgatga gctggggtct ggtgcagatg catctgcaac gcaggctgcc agatctacgg 6600
atgttgctgc tgtggtggtg cccatcttat tcctgatact gctgagcctg gggggtgggt 6660
ttgccatcct gtacacgaag caccggaggc tgcagagcag cttcaccgcc ttcgccaaca 6720
gccactacag ctccaggctg gggtccgcaa tcttctcctc tggggatgac ctgggggaag 6780
atgatgaaga tgcccctatg ataactggat tttcagatga cgtccccatg gtgatagcct 6840
gaaagagctt tcctcactag aaaccaaatg gtgtaaatat tttatttgat aaagatagtt 6900
gatggtttat tttaaaagat gcactttgag ttgcaatatg ttatttttat atgggccaaa 6960
aacaaaaaaa aaaaaaaaaa a                                                6981
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<210> 300
<211> 2214
<212> PRT
<213> Homo sapiens

<400> 300

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            20                  25                  30
Gln Arg Leu His Gly Gly Ser Ala Pro Leu Pro Gln Asp Arg Gly Phe
        35                  40                  45
Leu Val Val Gln Gly Asp Pro Arg Glu Leu Arg Leu Trp Ala Arg Gly
    50                  55                  60
Asp Ala Arg Gly Ala Ser Arg Ala Asp Glu Lys Pro Leu Arg Arg Lys
65                  70                  75                  80
Arg Ser Ala Ala Leu Gln Pro Glu Pro Ile Lys Val Tyr Gly Gln Val
                85                  90                  95
Ser Leu Asn Asp Ser His Asn Gln Met Val Val His Trp Ala Gly Glu
            100                 105                 110
Lys Ser Asn Val Ile Val Ala Leu Ala Arg Asp Ser Leu Ala Leu Ala
        115                 120                 125
Arg Pro Lys Ser Ser Asp Val Tyr Val Ser Tyr Asp Tyr Gly Lys Ser
    130                 135                 140
Phe Lys Lys Ile Ser Asp Lys Leu Asn Phe Gly Leu Gly Asn Arg Ser
145                 150                 155                 160
Glu Ala Val Ile Ala Gln Phe Tyr His Ser Pro Ala Asp Asn Lys Arg
                165                 170                 175
Tyr Ile Phe Ala Asp Ala Tyr Ala Gln Tyr Leu Trp Ile Thr Phe Asp
            180                 185                 190
Phe Cys Asn Thr Leu Gln Gly Phe Ser Ile Pro Phe Arg Ala Ala Asp
        195                 200                 205
Leu Leu Leu His Ser Lys Ala Ser Asn Leu Leu Leu Gly Phe Asp Arg
    210                 215                 220
Ser His Pro Asn Lys Gln Leu Trp Lys Ser Asp Asp Phe Gly Gln Thr
225                 230                 235                 240
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Trp Ile Met Ile Gln Glu His Val Lys Ser Phe Ser Trp Gly Ile Asp
                245                 250                 255
Pro Tyr Asp Lys Pro Asn Thr Ile Tyr Ile Glu Arg His Glu Pro Ser
            260                 265                 270
Gly Tyr Ser Thr Val Phe Arg Ser Thr Asp Phe Phe Gln Ser Arg Glu
        275                 280                 285
Asn Gln Glu Val Ile Leu Glu Glu Val Arg Asp Phe Gln Leu Arg Asp
    290                 295                 300
Lys Tyr Met Phe Ala Thr Lys Val Val His Leu Leu Gly Ser Glu Gln
305                 310                 315                 320
Gln Ser Ser Val Gln Leu Trp Val Ser Phe Gly Arg Lys Pro Met Arg
                325                 330                 335
Ala Ala Gln Phe Val Thr Arg His Pro Ile Asn Glu Tyr Tyr Ile Ala
            340                 345                 350
Asp Ala Ser Glu Asp Gln Val Phe Val Cys Val Ser His Ser Asn Asn
        355                 360                 365
Arg Thr Asn Leu Tyr Ile Ser Glu Ala Glu Gly Leu Lys Phe Ser Leu
    370                 375                 380
Ser Leu Glu Asn Val Leu Tyr Tyr Ser Pro Gly Gly Ala Gly Ser Asp
385                 390                 395                 400
Thr Leu Val Arg Tyr Phe Ala Asn Glu Pro Phe Ala Asp Phe His Arg
                405                 410                 415
Val Glu Gly Leu Gln Gly Val Tyr Ile Ala Thr Leu Ile Asn Gly Ser
            420                 425                 430
Met Asn Glu Glu Asn Met Arg Ser Val Ile Thr Phe Asp Lys Gly Gly
        435                 440                 445
Thr Trp Glu Phe Leu Gln Ala Pro Ala Phe Thr Gly Tyr Gly Glu Lys
    450                 455                 460
Ile Asn Cys Glu Leu Ser Gln Gly Cys Ser Leu His Leu Ala Gln Arg
465                 470                 475                 480
Leu Ser Gln Leu Leu Asn Leu Gln Leu Arg Arg Met Pro Ile Leu Ser
                485                 490                 495
Lys Glu Ser Ala Pro Gly Leu Ile Ile Ala Thr Gly Ser Val Gly Lys
            500                 505                 510
Asn Leu Ala Ser Lys Thr Asn Val Tyr Ile Ser Ser Ser Ala Gly Ala
        515                 520                 525
Arg Trp Arg Glu Ala Leu Pro Gly Pro His Tyr Tyr Thr Trp Gly Asp
    530                 535                 540
His Gly Gly Ile Ile Thr Ala Ile Ala Gln Gly Met Glu Thr Asn Glu
545                 550                 555                 560
Leu Lys Tyr Ser Thr Asn Glu Gly Glu Thr Trp Lys Thr Phe Ile Phe
                565                 570                 575
Ser Glu Lys Pro Val Phe Val Tyr Gly Leu Leu Thr Glu Pro Gly Glu
            580                 585                 590
Lys Ser Thr Val Phe Thr Ile Phe Gly Ser Asn Lys Glu Asn Val His
        595                 600                 605
Ser Trp Leu Ile Leu Gln Val Asn Ala Thr Asp Ala Leu Gly Val Pro
    610                 615                 620
Cys Thr Glu Asn Asp Tyr Lys Leu Trp Ser Pro Ser Asp Glu Arg Gly
625                 630                 635                 640
Asn Glu Cys Leu Leu Gly His Lys Thr Val Phe Lys Arg Arg Thr Pro
                645                 650                 655
His Ala Thr Cys Phe Asn Gly Glu Asp Phe Asp Arg Pro Val Val Val
            660                 665                 670
Ser Asn Cys Ser Cys Thr Arg Glu Asp Tyr Glu Cys Asp Phe Gly Phe
        675                 680                 685
Lys Met Ser Glu Asp Leu Ser Leu Glu Val Cys Val Pro Asp Pro Glu
    690                 695                 700
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Phe Ser Gly Lys Ser Tyr Ser Pro Pro Val Pro Cys Pro Val Gly Ser
705 710 715 720
Thr Tyr Arg Arg Thr Arg Gly Tyr Arg Lys Ile Ser Gly Asp Thr Cys
725 730 735
Ser Gly Gly Asp Val Glu Ala Arg Leu Glu Gly Glu Leu Val Pro Cys
740 745 750
Pro Leu Ala Glu Glu Asn Glu Phe Ile Leu Tyr Ala Val Arg Lys Ser
755 760 765
Ile Tyr Arg Tyr Asp Leu Ala Ser Gly Ala Thr Glu Gln Leu Pro Leu
770 775 780
Thr Gly Leu Arg Ala Ala Val Ala Leu Asp Phe Asp Tyr Glu His Asn
785 790 795 800
Cys Leu Tyr Trp Ser Asp Leu Ala Leu Asp Val Ile Gln Arg Leu Cys
805 810 815
Leu Asn Gly Ser Thr Gly Gln Glu Val Ile Ile Asn Ser Gly Leu Glu
820 825 830
Thr Val Glu Ala Leu Ala Phe Glu Pro Leu Ser Gln Leu Leu Tyr Trp
835 840 845
Val Asp Ala Gly Phe Lys Lys Ile Glu Val Ala Asn Pro Asp Gly Asp
850 855 860
Phe Arg Leu Thr Ile Val Asn Ser Ser Val Leu Asp Arg Pro Arg Ala
865 870 875 880
Leu Val Leu Val Pro Gln Glu Gly Val Met Phe Trp Thr Asp Trp Gly
885 890 895
Asp Leu Lys Pro Gly Ile Tyr Arg Ser Asn Met Asp Gly Ser Ala Ala
900 905 910
Tyr His Leu Val Ser Glu Asp Val Lys Trp Pro Asn Gly Ile Ser Val
915 920 925
Asp Asp Gln Trp Ile Tyr Trp Thr Asp Ala Tyr Leu Glu Cys Ile Glu
930 935 940
Arg Ile Thr Phe Ser Gly Gln Gln Arg Ser Val Ile Leu Asp Asn Leu
945 950 955 960
Pro His Pro Tyr Ala Ile Ala Val Phe Lys Asn Glu Ile Tyr Trp Asp
965 970 975
Asp Trp Ser Gln Leu Ser Ile Phe Arg Ala Ser Lys Tyr Ser Gly Ser
980 985 990
Gln Met Glu Ile Leu Ala Asn Gln Leu Thr Gly Leu Met Asp Met Lys
995 1000 1005
Ile Phe Tyr Lys Gly Lys Asn Thr Gly Ser Asn Ala Cys Val Pro Arg
1010 1015 1020
Pro Cys Ser Leu Leu Cys Leu Pro Lys Ala Asn Asn Ser Arg Ser Cys
1025 1030 1035 1040
Arg Cys Pro Glu Asp Val Ser Ser Ser Val Leu Pro Ser Gly Asp Leu
1045 1050 1055
Met Cys Asp Cys Pro Gln Gly Tyr Gln Leu Lys Asn Asn Thr Cys Val
1060 1065 1070
Lys Glu Glu Asn Thr Cys Leu Arg Asn Gln Tyr Arg Cys Ser Asn Gly
1075 1080 1085
Asn Cys Ile Asn Ser Ile Trp Trp Cys Asp Phe Asp Asn Asp Cys Gly
1090 1095 1100
Asp Met Ser Asp Glu Arg Asn Cys Pro Thr Thr Ile Cys Asp Leu Asp
1105 1110 1115 1120
Thr Gln Phe Arg Cys Gln Glu Ser Gly Thr Cys Ile Pro Leu Ser Tyr
1125 1130 1135
Lys Cys Asp Leu Glu Asp Asp Cys Gly Asp Asn Ser Asp Glu Ser His
1140 1145 1150
Cys Glu Met His Gln Cys Arg Ser Asp Glu Tyr Asn Cys Ser Ser Gly
1155 1160 1165

Met Cys Ile Arg Ser Ser Trp Val Cys Asp Gly Asp Asn Asp Cys Arg
1170 1175 1180
Asp Trp Ser Asp Glu Ala Asn Cys Thr Ala Ile Tyr His Thr Cys Glu
1185 1190 1195 1200
Ala Ser Asn Phe Gln Cys Arg Asn Gly His Cys Ile Pro Gln Arg Trp
1205 1210 1215
Ala Cys Asp Gly Asp Thr Asp Cys Gln Asp Gly Ser Asp Glu Asp Pro
1220 1225 1230
Val Asn Cys Glu Lys Lys Cys Asn Gly Phe Arg Cys Pro Asn Gly Thr
1235 1240 1245
Cys Ile Pro Ser Ser Lys His Cys Asp Gly Leu Arg Asp Cys Ser Asp
1250 1255 1260
Gly Ser Asp Glu Gln His Cys Glu Pro Leu Cys Thr His Phe Met Asp
1265 1270 1275 1280
Phe Val Cys Lys Asn Arg Gln Gln Cys Leu Phe His Ser Met Val Cys
1285 1290 1295
Asp Gly Ile Ile Gln Cys Arg Asp Gly Ser Asp Glu Asp Ala Ala Phe
1300 1305 1310
Ala Gly Cys Ser Gln Asp Pro Glu Phe His Lys Val Cys Asp Glu Phe
1315 1320 1325
Gly Phe Gln Cys Gln Asn Gly Val Cys Ile Ser Leu Ile Trp Lys Cys
1330 1335 1340
Asp Gly Met Asp Asp Cys Gly Asp Tyr Ser Asp Glu Ala Asn Cys Glu
1345 1350 1355 1360
Asn Pro Thr Glu Ala Pro Asn Cys Ser Arg Tyr Phe Gln Phe Arg Cys
1365 1370 1375
Glu Asn Gly His Cys Ile Pro Asn Arg Trp Lys Cys Asp Arg Glu Asn
1380 1385 1390
Asp Cys Gly Asp Trp Ser Asp Glu Lys Asp Cys Gly Asp Ser His Ile
1395 1400 1405
Leu Pro Phe Ser Thr Pro Gly Pro Ser Thr Cys Leu Pro Asn Tyr Tyr
1410 1415 1420
Arg Cys Ser Ser Gly Thr Cys Val Met Asp Thr Trp Val Cys Asp Gly
1425 1430 1435 1440
Tyr Arg Asp Cys Ala Asp Gly Ser Asp Glu Glu Ala Cys Pro Leu Leu
1445 1450 1455
Ala Asn Val Thr Ala Ala Ser Thr Pro Thr Gln Leu Gly Arg Cys Asp
1460 1465 1470
Arg Phe Glu Phe Glu Cys His Gln Pro Lys Thr Cys Ile Pro Asn Trp
1475 1480 1485
Lys Arg Cys Asp Gly His Gln Asp Cys Gln Asp Gly Arg Asp Glu Ala
1490 1495 1500
Asn Cys Pro Thr His Ser Thr Leu Thr Cys Met Ser Arg Glu Phe Gln
1505 1510 1515 1520
Cys Glu Asp Gly Glu Ala Cys Ile Val Leu Ser Glu Arg Cys Asp Gly
1525 1530 1535
Phe Leu Asp Cys Ser Asp Glu Ser Asp Glu Lys Ala Cys Ser Asp Glu
1540 1545 1550
Leu Thr Val Tyr Lys Val Gln Asn Leu Gln Trp Thr Ala Asp Phe Ser
1555 1560 1565
Gly Asp Val Thr Leu Thr Trp Met Arg Pro Lys Lys Met Pro Ser Ala
1570 1575 1580
Ser Cys Val Tyr Asn Val Tyr Tyr Arg Val Val Gly Glu Ser Ile Trp
1585 1590 1595 1600
Lys Thr Leu Glu Thr His Ser Asn Lys Thr Asn Thr Val Leu Lys Val
1605 1610 1615
Leu Lys Pro Asp Thr Thr Tyr Gln Val Lys Val Gln Val Gln Cys Leu
1620 1625 1630

Ser Lys Ala His Asn Thr Asn Asp Phe Val Thr Leu Arg Thr Pro Glu
        1635   1640   1645
Gly Leu Pro Asp Ala Pro Arg Asn Leu Gln Leu Ser Leu Pro Arg Glu
    1650   1655   1660
Ala Glu Gly Val Ile Val Gly His Trp Ala Pro Pro Ile His Thr His
1665   1670   1675   1680
Gly Leu Ile Arg Glu Tyr Ile Val Glu Tyr Ser Arg Ser Gly Ser Lys
                1685   1690   1695
Met Trp Ala Ser Gln Arg Ala Ala Ser Asn Phe Thr Glu Ile Lys Asn
            1700   1705   1710
Leu Leu Val Asn Thr Leu Tyr Thr Val Arg Val Ala Ala Val Thr Ser
        1715   1720   1725
Arg Gly Ile Gly Asn Trp Ser Asp Ser Lys Ser Ile Thr Thr Ile Lys
    1730   1735   1740
Gly Lys Val Ile Pro Pro Pro Asp Ile His Ile Asp Ser Tyr Gly Glu
1745   1750   1755   1760
Asn Tyr Leu Ser Phe Thr Leu Thr Met Glu Ser Asp Ile Lys Val Asn
                1765   1770   1775
Gly Tyr Val Val Asn Leu Phe Trp Ala Phe Asp Thr His Lys Gln Glu
            1780   1785   1790
Arg Arg Thr Leu Asn Phe Arg Gly Ser Ile Leu Ser His Lys Val Gly
        1795   1800   1805
Asn Leu Thr Ala His Thr Ser Tyr Glu Ile Ser Ala Trp Ala Lys Thr
    1810   1815   1820
Asp Leu Gly Asp Ser Pro Leu Ala Phe Glu His Val Met Thr Arg Gly
1825   1830   1835   1840
Val Arg Pro Pro Ala Pro Ser Leu Lys Ala Lys Ala Ile Asn Gln Thr
                1845   1850   1855
Ala Val Glu Cys Thr Trp Thr Gly Pro Arg Asn Val Val Tyr Gly Ile
            1860   1865   1870
Phe Tyr Ala Thr Ser Phe Leu Asp Leu Tyr Arg Asn Pro Lys Ser Leu
        1875   1880   1885
Thr Thr Ser Leu His Asn Lys Thr Val Ile Val Ser Lys Asp Glu Gln
    1890   1895   1900
Tyr Leu Phe Leu Val Arg Val Val Val Pro Tyr Gln Gly Pro Ser Ser
1905   1910   1915   1920
Asp Tyr Val Val Val Lys Met Ile Pro Asp Ser Arg Leu Pro Pro Arg
                1925   1930   1935
His Leu His Val Val His Thr Gly Lys Thr Ser Val Val Ile Lys Trp
            1940   1945   1950
Glu Ser Pro Tyr Asp Ser Pro Asp Gln Asp Leu Leu Tyr Ala Ile Ala
        1955   1960   1965
Val Lys Asp Leu Ile Arg Lys Thr Asp Arg Ser Tyr Lys Val Lys Ser
    1970   1975   1980
Arg Asn Ser Thr Val Glu Tyr Thr Leu Asn Lys Leu Glu Pro Gly Gly
1985   1990   1995   2000
Lys Tyr His Ile Ile Val Gln Leu Gly Asn Met Ser Lys Asp Ser Ser
                2005   2010   2015
Ile Lys Ile Thr Thr Val Ser Leu Ser Ala Pro Asp Ala Leu Lys Ile
            2020   2025   2030
Ile Thr Glu Asn Asp His Val Leu Leu Phe Trp Lys Ser Leu Ala Leu
        2035   2040   2045
Lys Glu Lys His Phe Asn Glu Ser Arg Gly Tyr Glu Ile His Met Phe
    2050   2055   2060
Asp Ser Ala Met Asn Ile Thr Ala Tyr Leu Gly Asn Thr Thr Asp Asn
2065   2070   2075   2080
Phe Phe Lys Ile Ser Asn Leu Lys Met Gly His Asn Tyr Thr Phe Thr
                2085   2090   2095

Val Gln Ala Arg Cys Leu Phe Gly Asn Gln Ile Cys Gly Glu Pro Ala
2100 2105 2110
Ile Leu Leu Tyr Asp Glu Leu Gly Ser Gly Ala Asp Ala Ser Ala Thr
2115 2120 2125
Gln Ala Ala Arg Ser Thr Asp Val Ala Ala Val Val Pro Ile Leu
2130 2135 2140
Phe Leu Ile Leu Leu Ser Leu Gly Val Gly Phe Ala Ile Leu Tyr Thr
2145 2150 2155 2160
Lys His Arg Arg Leu Gln Ser Ser Phe Thr Ala Phe Ala Asn Ser His
2165 2170 2175
Tyr Ser Ser Arg Leu Gly Ser Ala Ile Phe Ser Ser Gly Asp Asp Leu
2180 2185 2190
Gly Glu Asp Asp Glu Asp Ala Pro Met Ile Thr Gly Phe Ser Asp Asp
2195 2200 2205
Val Pro Met Val Ile Ala
2210

<210> 301
<211> 1544
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1544)
<223> n = A,T,C or G

<400> 301
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cggcgagggc gcgagtgagg agcagaccca ggcatcgcgc gccgagaagg ccgggcgtcc 120
ccacactgaa ggtccggaaa ggcgacttcc gggggctttg gcacctggcg gaccctcccg 180
gagcgtcggc acctgaacgc gaggcgctcc attgcgcgtg cgcgttgagg ggcttcccgc 240
acctgatcgc gagaccccaa cggctggtgg cgtcgcctgc gcgtctcggc tgagctggcc 300
atggcgcagc tgtgcgggct gaggcggagc cgggcgtttc tcgccctgct gggatcgctg 360
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tcgaaggtgg tgggcagatg ccgggcctcc atgcctaggt ggtggtacaa tgtcactgac 480
ggatcctgcc agctgtttgt gtatgggggc tgtgacggaa acagcaataa ttacctgacc 540
aaggaggagt gcctcaagaa atgtgccact gtcacagaga atgccacggg tgacctggcc 600
accagcagga atgcagcgga ttcctctgtc ccaagtgctc ccagaaggca ggattctgaa 660
gaccactcca gcgatatgtt caactatgaa gaatactgca ccgccaacgc agtcactggg 720
ccttgccgtg catccttccc acgctggtac tttgacgtgg agaggaactc ctgcaataac 780
ttcatctatg gaggctgccg gggcaataag aacagctacc gctctgagga ggcctgcatg 840
ctccgctgct tccgccagca ggagaatcct cccctgcccc ttggctcaaa ggtggtggtt 900
ctggcggggc tgttcgtgat ggtgttgatc ctcttcctgg gagcctccat ggtctacctg 960
atccgggtgg cacggaggaa ccaggagcgt gccctgcgca ccgtctggag ctccggagat 1020
gacaaggagc agctggtgaa gaacacatat gtcctgtgac cgccctgtcg ccaagaggac 1080
tggggaaggg aggggagact atgtgtgagc ttttttaaa tagagggatt gactcggatt 1140
tgagtgatca ttagggctga ggtctgtttc tctgggaggt aggacggctg cttcctggtc 1200
tggcagggat gggtttgctt tggaaatcct ctaggaggct cctcctcgca tggcctgcag 1260
tctggcagca gccccgagtt gtttcctcgc tgatcgattt ctttcctcca ggtagagttt 1320
tctttgctta tgttgaattc cattgcctcc ttttctcnat cacagaagtg atgttggaat 1380
cgtttctttt gtttgtctga tttatggttt ttttaagtat aaacaaaagt tttttattag 1440
cattctgaaa gaaggaaagt aaaatgtaca agtttaataa aaaggggcct tcccctttag 1500
aataaatttc cagcatgttg ctttcaaaaa aaaaaaaaaa aaaa 1544

<210> 302
<211> 252

<212> PRT
<213> Homo sapiens

<400> 302
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Leu Gly Ser Leu Leu Leu Ser Gly Val Leu Ala Ala Asp Arg Glu Arg
20 25 30
Ser Ile His Asp Phe Cys Leu Val Ser Lys Val Val Gly Arg Cys Arg
35 40 45
Ala Ser Met Pro Arg Trp Trp Tyr Asn Val Thr Asp Gly Ser Cys Gln
50 55 60
Leu Phe Val Tyr Gly Gly Cys Asp Gly Asn Ser Asn Asn Tyr Leu Thr
65 70 75 80
Lys Glu Glu Cys Leu Lys Lys Cys Ala Thr Val Thr Glu Asn Ala Thr
85 90 95
Gly Asp Leu Ala Thr Ser Arg Asn Ala Ala Asp Ser Ser Val Pro Ser
100 105 110
Ala Pro Arg Arg Gln Asp Ser Glu Asp His Ser Ser Asp Met Phe Asn
115 120 125
Tyr Glu Glu Tyr Cys Thr Ala Asn Ala Val Thr Gly Pro Cys Arg Ala
130 135 140
Ser Phe Pro Arg Trp Tyr Phe Asp Val Glu Arg Asn Ser Cys Asn Asn
145 150 155 160
Phe Ile Tyr Gly Gly Cys Arg Gly Asn Lys Asn Ser Tyr Arg Ser Glu
165 170 175
Glu Ala Cys Met Leu Arg Cys Phe Arg Gln Gln Glu Asn Pro Pro Leu
180 185 190
Pro Leu Gly Ser Lys Val Val Val Leu Ala Gly Leu Phe Val Met Val
195 200 205
Leu Ile Leu Phe Leu Gly Ala Ser Met Val Tyr Leu Ile Arg Val Ala
210 215 220
Arg Arg Asn Gln Glu Arg Ala Leu Arg Thr Val Trp Ser Ser Gly Asp
225 230 235 240
Asp Lys Glu Gln Leu Val Lys Asn Thr Tyr Val Leu
245 250

<210> 303
<211> 1558
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1558)
<223> n = A,T,C or G

<400> 303
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gaacgcgctg agggccgttg agtgtcgcag gcggcgaggg cgcgagtgag gagcagaccc 120
aggcatcgcg cgccgagaag gccgggcgtc cccacactga aggtccggaa aggcgacttc 180
cgggggcttt ggcacctggc ggaccctccc ggagcgtcgg cacctgaacg cgaggcgctc 240
cattgcgcgt gcgcgttgag ggcttcccg cacctgatcg cgagacccca acggctggtg 300
gcgtcgcctg cgcgtctcgg ctgagctggc catggcgcag ctgtgcgggc tgaggcggag 360
ccgggcgttt ctcgccctgc tgggatcgct gctcctctct ggggtcctgg cggccgaccg 420
agaacgcagc atccacgaga atgccacggg tgacctggcc accagcagga atgcagcgga 480
ttcctctgtc ccaagtgctc ccagaaggca ggattctgaa gaccactcca gcgatatgtt 540

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caactatgaa gaatactgca ccgccaacgc agtcactggg ccttgccgtg catccttccc 600
acgctggtac tttgacgtgg agaggaactc ctgcaataac ttcatctatg gaggctgccg 660
gggcaataag aacagctacc gctctgagga ggcctgcatg ctccgctgct tccgccagca 720
ggagaatcct cccctgcccc ttggctcaaa ggtggtgstt ctggcggggc tgttcgtgat 780
ggtgttgatc ctcttcctgg gagcctccat ggtctacctg atccgggtgg cacggaggaa 840
ccaggagcgt gccctgcgca ccgtctggag ctccggagat gacaaggagc agctggtgaa 900
gaacacatat gtcctgtgac cgccctgtcg ccaagaggac tggggaaggg aggggagact 960
atgtgtgagc tttttttaaa tagagggatt gactcggatt tgagtgatca ttagggctga 1020
ggtctgtttc tctgggaggt aggacggctg cttcctggtc tggcagggat gggtttgctt 1080
tggaaatcct ctaggaggct cctcctcgca tggcctgcag tctggcagca gccccgagtt 1140
gtttcctcgc tgatcgattt ctttcctcca ggtagagttt tctttgctta tgttgaattc 1200
cattgcctct tttctcatca cagaagtgat gttggaatcg tttcttttgt ttgtctgatt 1260
tatggttttt ttaagtataa acaaaagttt tttattagca ttctgaaaga aggaaagtaa 1320
aatgtacctn cgcccgnnnc ganccrctcg amcbttccch htaraawaaa wwwmarmawr 1380
tgctttcttt atgggagtcc taatttcaac cctaccaaaa tgatcacaag acactatctg 1440
aggtgtccca ttctagaaat agacccctca aaatagcgtc tttcagatct ttttgaatga 1500
atccacaaga tgaaataaat gtcctattac tgaaaaaaaa aaaaaaaagg gcggccgc   1558
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<210> 304
<211> 195
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> (1)...(195)
<223> Xaa = Any Amino Acid

<400> 304

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            20                  25                  30
Ser Ile His Glu Asn Ala Thr Gly Asp Leu Ala Thr Ser Arg Asn Ala
        35                  40                  45
Ala Asp Ser Ser Val Pro Ser Ala Pro Arg Arg Gln Asp Ser Glu Asp
    50                  55                  60
His Ser Ser Asp Met Phe Asn Tyr Glu Glu Tyr Cys Thr Ala Asn Ala
65                  70                  75                  80
Val Thr Gly Pro Cys Arg Ala Ser Phe Pro Arg Trp Tyr Phe Asp Val
                85                  90                  95
Glu Arg Asn Ser Cys Asn Asn Phe Ile Tyr Gly Gly Cys Arg Gly Asn
            100                 105                 110
Lys Asn Ser Tyr Arg Ser Glu Glu Ala Cys Met Leu Arg Cys Phe Arg
        115                 120                 125
Gln Gln Glu Asn Pro Pro Leu Pro Leu Gly Ser Lys Val Val Xaa Leu
    130                 135                 140
Ala Gly Leu Phe Val Met Val Leu Ile Leu Phe Leu Gly Ala Ser Met
145                 150                 155                 160
Val Tyr Leu Ile Arg Val Ala Arg Arg Asn Gln Glu Arg Ala Leu Arg
                165                 170                 175
Thr Val Trp Ser Ser Gly Asp Asp Lys Glu Gln Leu Val Lys Asn Thr
            180                 185                 190
Tyr Val Leu
        195
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<210> 305

<211> 3079
<212> DNA
<213> Homo sapiens

<400> 305
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<400> 307

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<210> 310
<211> 835
<212> PRT
<213> Homo sapiens

<400> 310

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            20                  25                  30
Cys Ala Gly Gly Ser Gly Gln Asn Gln Pro Ser Leu Leu Pro Leu Leu
        35                  40                  45
Arg Arg Gly Pro Pro Leu Leu Ala Leu Leu Ser Phe Ala Trp Leu Ser
    50                  55                  60
Ser Ala Gln Leu Ser Ala Ala Pro Arg Pro Pro Ser Arg Gly Gly His
65                  70                  75                  80
Gly Leu Arg Val Ala Asp Ala Ser Ser Glu Leu Pro Leu Ser Ala Ala
                85                  90                  95
Pro Pro Pro Gly Arg Ala Phe Val Gly Thr Thr Ser Gly Arg Ser Arg
            100                 105                 110
Val Ala Lys Ala Cys Gly Arg Gly Thr Lys Leu Gly Ala Ala Lys Met
        115                 120                 125
Arg Leu Ser Pro Ala Pro Leu Lys Leu Ser Arg Thr Pro Ala Leu Leu
    130                 135                 140
Ala Leu Ala Leu Pro Leu Ala Ala Ala Leu Ala Phe Ser Asp Glu Thr
145                 150                 155                 160
Leu Asp Lys Val Pro Lys Ser Glu Gly Tyr Cys Ser Arg Ile Leu Arg
                165                 170                 175
Ala Gln Gly Thr Arg Arg Glu Gly Tyr Thr Glu Phe Ser Leu Arg Val
            180                 185                 190
Glu Gly Asp Pro Asp Phe Tyr Lys Pro Gly Thr Ser Tyr Arg Val Thr
        195                 200                 205
Leu Ser Ala Ala Pro Pro Ser Tyr Phe Arg Gly Phe Thr Leu Ile Ala
    210                 215                 220
Leu Arg Glu Asn Arg Glu Gly Asp Lys Glu Glu Asp His Ala Gly Thr
225                 230                 235                 240
```

```
Phe Gln Ile Ile Asp Glu Glu Glu Thr Gln Phe Met Ser Asn Cys Pro
                245                 250                 255
Val Ala Val Thr Glu Ser Thr Pro Arg Arg Arg Thr Arg Ile Gln Val
            260                 265                 270
Phe Trp Ile Ala Pro Pro Ala Gly Thr Gly Cys Val Ile Leu Lys Ala
        275                 280                 285
Ser Ile Val Gln Lys Arg Ile Ile Tyr Phe Gln Asp Glu Gly Ser Leu
    290                 295                 300
Thr Lys Lys Leu Cys Glu Gln Asp Ser Thr Phe Asp Gly Val Thr Asp
305                 310                 315                 320
Lys Pro Ile Leu Asp Cys Cys Ala Cys Gly Thr Ala Lys Tyr Arg Leu
                325                 330                 335
Thr Phe Tyr Gly Asn Trp Ser Glu Lys Thr His Pro Lys Asp Tyr Pro
            340                 345                 350
Arg Arg Ala Asn His Trp Ser Ala Ile Ile Gly Gly Ser His Ser Lys
        355                 360                 365
Asn Tyr Val Leu Trp Glu Tyr Gly Gly Tyr Ala Ser Glu Gly Val Lys
    370                 375                 380
Gln Val Ala Glu Leu Gly Ser Pro Val Lys Met Glu Glu Glu Ile Arg
385                 390                 395                 400
Gln Gln Ser Asp Glu Val Leu Thr Val Ile Lys Ala Lys Ala Gln Trp
                405                 410                 415
Pro Ala Trp Gln Pro Leu Asn Val Arg Ala Ala Pro Ser Ala Glu Phe
            420                 425                 430
Ser Val Asp Arg Thr Arg His Leu Met Ser Phe Leu Thr Met Met Gly
        435                 440                 445
Pro Ser Pro Asp Trp Asn Val Gly Leu Ser Ala Glu Asp Leu Cys Thr
    450                 455                 460
Lys Glu Cys Gly Trp Val Gln Lys Val Val Gln Asp Leu Ile Pro Trp
465                 470                 475                 480
Asp Ala Gly Thr Asp Ser Gly Val Thr Tyr Glu Ser Pro Asn Lys Pro
                485                 490                 495
Thr Ile Pro Gln Glu Lys Ile Arg Pro Leu Thr Ser Leu Asp His Pro
            500                 505                 510
Gln Ser Pro Phe Tyr Asp Pro Glu Gly Gly Ser Ile Thr Gln Val Ala
        515                 520                 525
Arg Val Val Ile Glu Arg Ile Ala Arg Lys Gly Glu Gln Cys Asn Ile
    530                 535                 540
Val Pro Asp Asn Val Asp Asp Ile Val Ala Asp Leu Ala Pro Glu Glu
545                 550                 555                 560
Lys Asp Glu Asp Asp Thr Pro Glu Thr Cys Ile Tyr Ser Asn Trp Ser
                565                 570                 575
Pro Trp Ser Ala Cys Ser Ser Ser Thr Cys Asp Lys Gly Lys Arg Met
            580                 585                 590
Arg Gln Arg Met Leu Lys Ala Gln Leu Asp Leu Ser Val Pro Cys Pro
        595                 600                 605
Asp Thr Gln Asp Phe Gln Pro Cys Met Gly Pro Gly Cys Ser Asp Glu
    610                 615                 620
Asp Gly Ser Thr Cys Thr Met Ser Glu Trp Ile Thr Trp Ser Pro Cys
625                 630                 635                 640
Ser Ile Ser Cys Gly Met Gly Met Arg Ser Arg Glu Arg Tyr Val Lys
                645                 650                 655
Gln Phe Pro Glu Asp Gly Ser Val Cys Thr Leu Pro Thr Glu Glu Thr
            660                 665                 670
Glu Lys Cys Thr Val Asn Glu Glu Cys Ser Pro Ser Ser Cys Leu Met
        675                 680                 685
Thr Glu Trp Gly Glu Trp Asp Glu Cys Ser Ala Thr Cys Gly Met Gly
    690                 695                 700
```

```
Met Lys Lys Arg His Arg Met Ile Lys Met Asn Pro Ala Asp Gly Ser
705                 710                 715                 720
Met Cys Lys Ala Glu Thr Ser Gln Ala Glu Lys Cys Met Met Pro Glu
                725                 730                 735
Cys His Thr Ile Pro Cys Leu Leu Ser Pro Trp Ser Glu Trp Ser Asp
            740                 745                 750
Cys Ser Val Thr Cys Gly Lys Gly Met Arg Thr Arg Gln Arg Met Leu
        755                 760                 765
Lys Ser Leu Ala Glu Leu Gly Asp Cys Asn Glu Asp Leu Glu Gln Val
    770                 775                 780
Glu Lys Cys Met Leu Pro Glu Cys Pro Ile Asp Cys Glu Leu Thr Glu
785                 790                 795                 800
Trp Ser Gln Trp Ser Glu Cys Asn Lys Ser Cys Gly Lys Gly His Val
                805                 810                 815
Ile Arg Thr Arg Met Ile Gln Met Glu Pro Gln Phe Leu Gln Ser Leu
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Leu Glu Ser
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<210> 311
<211> 3112
<212> DNA
<213> Homo sapiens

<400> 311

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<210> 312
<211> 782
<212> PRT
<213> Homo sapiens

<400> 312

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            20                  25                  30
Glu Glu Gly Val Glu Phe Leu Pro Val Asn Asn Val Lys Lys Val Glu
        35                  40                  45
Lys His Gly Pro Gly Arg Trp Val Val Leu Ala Ala Val Leu Ile Gly
    50                  55                  60
Leu Leu Leu Val Leu Leu Gly Ile Gly Phe Leu Val Trp His Leu Gln
65                  70                  75                  80
Tyr Arg Asp Val Arg Val Gln Lys Val Phe Asn Gly Tyr Met Arg Ile
                85                  90                  95
Thr Asn Glu Asn Phe Val Asp Ala Tyr Glu Asn Ser Asn Ser Thr Glu
            100                 105                 110
Phe Val Ser Leu Ala Ser Lys Val Lys Asp Ala Leu Lys Leu Leu Tyr
        115                 120                 125
Ser Gly Val Pro Phe Leu Gly Pro Tyr His Lys Glu Ser Ala Val Thr
    130                 135                 140
Ala Phe Ser Glu Gly Ser Val Ile Ala Tyr Tyr Trp Ser Glu Phe Ser
145                 150                 155                 160
Ile Pro Gln His Leu Val Glu Glu Ala Glu Arg Val Met Ala Glu Glu
                165                 170                 175
Arg Val Val Met Leu Pro Pro Arg Ala Arg Ser Leu Lys Ser Phe Val
            180                 185                 190
Val Thr Ser Val Val Ala Phe Pro Thr Asp Ser Lys Thr Val Gln Arg
        195                 200                 205
Thr Gln Asp Asn Ser Cys Ser Phe Gly Leu His Ala Arg Gly Val Glu
    210                 215                 220
Leu Met Arg Phe Thr Thr Pro Gly Phe Pro Asp Ser Pro Tyr Pro Ala
225                 230                 235                 240
His Ala Arg Cys Gln Trp Ala Leu Arg Gly Asp Ala Asp Ser Val Leu
```

```
                245                 250                 255
Ser Leu Thr Phe Arg Ser Phe Asp Leu Ala Ser Cys Asp Glu Arg Gly
            260                 265                 270
Ser Asp Leu Val Thr Val Tyr Asn Thr Leu Ser Pro Met Glu Pro His
        275                 280                 285
Ala Leu Val Gln Leu Cys Gly Thr Tyr Pro Pro Ser Tyr Asn Leu Thr
    290                 295                 300
Phe His Ser Ser Gln Asn Val Leu Leu Ile Thr Leu Ile Thr Asn Thr
305                 310                 315                 320
Glu Arg Arg His Pro Gly Phe Glu Ala Thr Phe Phe Gln Leu Pro Arg
                325                 330                 335
Met Ser Ser Cys Gly Gly Arg Leu Arg Lys Ala Gln Gly Thr Phe Asn
            340                 345                 350
Ser Pro Tyr Tyr Pro Gly His Tyr Pro Pro Asn Ile Asp Cys Thr Trp
        355                 360                 365
Asn Ile Glu Val Pro Asn Asn Gln His Val Lys Val Arg Phe Lys Phe
    370                 375                 380
Phe Tyr Leu Leu Glu Pro Gly Val Pro Ala Gly Thr Cys Pro Lys Asp
385                 390                 395                 400
Tyr Val Glu Ile Asn Gly Glu Lys Tyr Cys Gly Glu Arg Ser Gln Phe
                405                 410                 415
Val Val Thr Ser Asn Ser Asn Lys Ile Thr Val Arg Phe His Ser Asp
            420                 425                 430
Gln Ser Tyr Thr Asp Thr Gly Phe Leu Ala Glu Tyr Leu Ser Tyr Asp
        435                 440                 445
Ser Ser Asp Arg Cys Asp Ala Gly His Gln Phe Thr Cys Lys Asn Lys
    450                 455                 460
Phe Cys Lys Pro Leu Phe Trp Val Cys Asp Ser Val Asn Asp Cys Gly
465                 470                 475                 480
Asp Asn Ser Asp Glu Gln Gly Cys Met Asn Val Val Thr Cys Thr Lys
                485                 490                 495
His Thr Tyr Arg Cys Leu Asn Gly Leu Cys Leu Ser Lys Gly Asn Pro
            500                 505                 510
Glu Cys Asp Gly Lys Glu Asp Cys Ser Asp Gly Ser Asp Glu Lys Asp
        515                 520                 525
Cys Asp Cys Gly Leu Arg Ser Phe Thr Arg Gln Ala Arg Val Val Gly
    530                 535                 540
Gly Thr Asp Ala Asp Glu Gly Glu Trp Pro Trp Gln Val Ser Leu His
545                 550                 555                 560
Ala Leu Gly Gln Gly His Ile Cys Gly Ala Ser Leu Ile Ser Pro Asn
                565                 570                 575
Trp Leu Val Ser Ala Ala His Cys Tyr Ile Asp Asp Arg Gly Phe Arg
            580                 585                 590
Tyr Ser Asp Pro Thr Gln Trp Thr Ala Phe Leu Gly Leu His Asp Gln
        595                 600                 605
Ser Gln Arg Ser Ala Pro Gly Val Gln Glu Arg Arg Leu Lys Arg Ile
    610                 615                 620
Ile Ser His Pro Phe Phe Asn Asp Phe Thr Phe Asp Tyr Asp Ile Ala
625                 630                 635                 640
Leu Leu Glu Leu Glu Lys Pro Ala Glu Tyr Ser Ser Met Val Arg Pro
                645                 650                 655
Ile Cys Leu Pro Asp Ala Ser His Val Phe Pro Ala Gly Lys Ala Ile
            660                 665                 670
Trp Val Thr Gly Trp Gly His Thr Gln Tyr Gly Gly Thr Gly Ala Leu
        675                 680                 685
Ile Leu Gln Lys Gly Glu Ile Arg Val Ile Asn Gln Thr Thr Cys Glu
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Asn Leu Leu Pro Gln Gln Ile Thr Pro Arg Met Met Cys Val Gly Phe
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705                 710                 715                 720
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Ser Ser Val Glu Ala Asp Gly Arg Ile Phe Gln Ala Gly Val Val Ser
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<210> 313
<211> 2805
<212> DNA
<213> Homo sapiens

<400> 313

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<211> 323
<212> PRT
<213> Homo sapiens

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35 40 45
Pro Gly Gly Arg Cys Gln Cys Arg Ala Leu Gly Ser Gly Met Ala Val
50 55 60
Asp Cys Ser Thr Leu Thr Ser Lys Cys Leu Leu Leu Lys Ala Arg Met
65 70 75 80
Ser Ala Pro Lys Asn Ala Arg Thr Leu Val Arg Pro Ser Glu His Ala
85 90 95
Leu Val Asp Asn Asp Gly Leu Tyr Asp Pro Asp Cys Asp Pro Glu Gly
100 105 110
Arg Phe Lys Ala Arg Gln Cys Asn Gln Thr Ser Val Cys Trp Cys Val
115 120 125
Asn Ser Val Gly Val Arg Arg Thr Asp Lys Gly Asp Leu Ser Leu Arg
130 135 140
Cys Asp Glu Leu Val Arg Thr His His Ile Leu Ile Asp Leu Arg His
145 150 155 160
Arg Pro Thr Ala Gly Ala Phe Asn His Ser Asp Leu Asp Ala Glu Leu
165 170 175
Arg Arg Leu Phe Arg Glu Arg Tyr Arg Leu His Pro Lys Phe Val Ala
180 185 190
Ala Val His Tyr Glu Gln Pro Thr Ile Gln Ile Glu Leu Arg Gln Asn
195 200 205
Thr Ser Gln Lys Ala Ala Gly Glu Val Asp Ile Gly Asp Ala Ala Tyr
210 215 220
Tyr Phe Glu Arg Asp Ile Lys Gly Glu Ser Leu Phe Gln Gly Arg Gly
225 230 235 240
Gly Leu Asp Leu Arg Val Arg Gly Glu Pro Leu Gln Val Glu Arg Thr
245 250 255
Leu Ile Tyr Tyr Leu Asp Glu Ile Pro Pro Lys Phe Ser Met Lys Arg
260 265 270
Leu Thr Ala Gly Leu Ile Ala Val Ile Val Val Val Val Val Ala Leu
275 280 285
Val Ala Gly Met Ala Val Leu Val Ile Thr Asn Arg Arg Lys Ser Gly
290 295 300
Lys Tyr Lys Lys Val Glu Ile Lys Glu Leu Gly Glu Leu Arg Lys Glu
305 310 315 320
Pro Ser Leu

<210> 315

<211> 1142
<212> DNA
<213> Homo sapiens

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<210> 316
<211> 235
<212> PRT
<213> Homo sapiens

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35 40 45
Leu Leu Arg Tyr Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe
50 55 60
Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu
65 70 75 80
Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys
85 90 95
Arg Leu Gln Val Ser Val Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys
100 105 110
Tyr Phe Phe Asn Leu Ser Ser Met Thr Cys Glu Lys Phe Phe Ser Gly
115 120 125
Gly Cys His Arg Asn Arg Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr
130 135 140
Cys Met Gly Phe Cys Ala Pro Lys Lys Ile Pro Ser Phe Cys Tyr Ser
145 150 155 160
Pro Lys Asp Glu Gly Leu Cys Ser Ala Asn Val Thr Arg Tyr Tyr Phe
165 170 175
Asn Pro Arg Tyr Arg Thr Cys Asp Ala Phe Thr Tyr Thr Gly Cys Gly
180 185 190
Gly Asn Asp Asn Asn Phe Val Ser Arg Glu Asp Cys Lys Arg Ala Cys
195 200 205

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225                 230                 235
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<210> 317
<211> 2307
<212> DNA
<213> Homo sapiens

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<400> 317

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<210> 318

<211> 428
<212> PRT
<213> Homo sapiens

<400> 318
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35 40 45
Val Val Val Leu Ile Lys Val Ile Leu Asp Lys Tyr Tyr Phe Leu Cys
50 55 60
Gly Gln Pro Leu His Phe Ile Pro Arg Lys Gln Leu Cys Asp Gly Glu
65 70 75 80
Leu Asp Cys Pro Leu Gly Glu Asp Glu Glu His Cys Val Lys Ser Phe
85 90 95
Pro Glu Gly Pro Ala Val Ala Val Arg Leu Ser Lys Asp Arg Ser Thr
100 105 110
Leu Gln Val Leu Asp Ser Ala Thr Gly Asn Trp Phe Ser Ala Cys Phe
115 120 125
Asp Asn Phe Thr Glu Ala Leu Ala Glu Thr Ala Cys Arg Gln Met Gly
130 135 140
Tyr Ser Ser Lys Pro Thr Phe Arg Ala Val Glu Ile Gly Pro Asp Gln
145 150 155 160
Asp Leu Asp Val Val Glu Ile Thr Glu Asn Ser Gln Glu Leu Arg Met
165 170 175
Arg Asn Ser Ser Gly Pro Cys Leu Ser Gly Ser Leu Val Ser Leu His
180 185 190
Cys Leu Ala Cys Gly Lys Ser Leu Lys Thr Pro Arg Val Val Gly Gly
195 200 205
Glu Glu Ala Ser Val Asp Ser Trp Pro Trp Gln Val Ser Ile Gln Tyr
210 215 220
Asp Lys Gln His Val Cys Gly Gly Ser Ile Leu Asp Pro His Trp Val
225 230 235 240
Leu Thr Ala Ala His Cys Phe Arg Lys His Thr Asp Val Phe Asn Trp
245 250 255
Lys Val Arg Ala Gly Ser Asp Lys Leu Gly Ser Phe Pro Ser Leu Ala
260 265 270
Val Ala Lys Ile Ile Ile Ile Glu Phe Asn Pro Met Tyr Pro Lys Asp
275 280 285
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Thr Val Arg Pro Ile Cys Leu Pro Phe Phe Asp Glu Glu Leu Thr Pro
305 310 315 320
Ala Thr Pro Leu Trp Ile Ile Gly Trp Gly Phe Thr Lys Gln Asn Gly
325 330 335
Gly Lys Met Ser Asp Ile Leu Leu Gln Ala Ser Val Gln Val Ile Asp
340 345 350
Ser Thr Arg Cys Asn Ala Asp Asp Ala Tyr Gln Gly Glu Val Thr Glu
355 360 365
Lys Met Met Cys Ala Gly Ile Pro Glu Gly Gly Val Asp Thr Cys Gln
370 375 380
Gly Asp Ser Gly Gly Pro Leu Met Tyr Gln Ser Asp Gln Trp His Val
385 390 395 400
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Gly Val Tyr Thr Lys Val Ser Ala Tyr Leu Asn Trp

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<210> 319
<211> 3529
<212> DNA
<213> Homo sapiens

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<210> 320
<211> 444
<212> PRT
<213> Homo sapiens

<400> 320
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Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
        35                  40                  45
Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
    50                  55                  60
Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
65                  70                  75                  80
Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
                85                  90                  95
Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
            100                 105                 110
Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
        115                 120                 125
Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
    130                 135                 140
Arg Lys Tyr Phe Ala Asp Leu Ala Met Asn Tyr Lys His Gly Asp Pro
145                 150                 155                 160
Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
                165                 170                 175
Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
            180                 185                 190
Tyr Leu Lys Asn Leu Pro Leu Leu Ser Lys Tyr Cys Gly Tyr Arg Glu
        195                 200                 205
Asp Asn Ile Pro Gln Leu Glu Asp Val Ser Asn Phe Leu Lys Glu Arg
    210                 215                 220
Thr Gly Phe Ser Ile Arg Pro Val Ala Gly Tyr Leu Ser Pro Arg Asp
225                 230                 235                 240
Phe Leu Ser Gly Leu Ala Phe Arg Val Phe His Cys Thr Gln Tyr Val
                245                 250                 255
Arg His Ser Ser Asp Pro Phe Tyr Thr Pro Glu Pro Asp Thr Cys His
            260                 265                 270
Glu Leu Leu Gly His Val Pro Leu Leu Ala Glu Pro Ser Phe Ala Gln
        275                 280                 285
Phe Ser Gln Glu Ile Gly Leu Ala Ser Leu Gly Ala Ser Glu Glu Ala
    290                 295                 300
Val Gln Lys Leu Ala Thr Cys Tyr Phe Phe Thr Val Glu Phe Gly Leu
305                 310                 315                 320
Cys Lys Gln Asp Gly Gln Leu Arg Val Phe Gly Ala Gly Leu Leu Ser
```

325 330 335
Ser Ile Ser Glu Leu Lys His Ala Leu Ser Gly His Ala Lys Val Lys
340 345 350
Pro Phe Asp Pro Lys Ile Thr Cys Lys Gln Glu Cys Leu Ile Thr Thr
355 360 365
Phe Gln Asp Val Tyr Phe Val Ser Glu Ser Phe Glu Asp Ala Lys Glu
370 375 380
Lys Met Arg Glu Phe Thr Lys Thr Ile Lys Arg Pro Phe Gly Val Lys
385 390 395 400
Tyr Asn Pro Tyr Thr Arg Ser Ile Gln Ile Leu Lys Asp Thr Lys Ser
405 410 415
Ile Thr Ser Ala Met Asn Glu Leu Gln His Asp Leu Asp Val Val Ser
420 425 430
Asp Ala Leu Ala Lys Val Ser Arg Lys Pro Ser Ile
435 440

<210> 321
<211> 3505
<212> DNA
<213> Homo sapiens

<400> 321
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atttttcct taaagaatga agttggagga cttataaaag ccctgaaaat ctttcaggag 120
aagcatgtga atctgttaca tatcgagtcc cgaaaatcaa aaagaagaaa ctcagaattt 180
gagattttg ttgactgtga catcaacaga gaacaattga atgatatttt tcatctgctg 240
aagtctcata ccaatgttct ctctgtgaat ctaccagata attttacttt gaaggaagat 300
ggtatggaaa ctgttccttg gtttccaaag aagatttctg acctggacca ttgtgccaac 360
agagttctga tgtatggatc tgaactagat gcagaccatc ctggcttcaa agacaatgtc 420
taccgtaaac gtcgaaagta ttttgcggac ttggctatga actataaaca tggagacccc 480
attccaaagg ttgaattcac tgaagaggag attaagacct ggggaaccgt attccaagag 540
ctcaacaaac tctacccaac ccatgcttgc agagagtatc tcaaaaactt acctttgctt 600
tctaaatatt gtggatatcg ggaggataat atcccacaat tggaagatgt ctccaacttt 660
ttaaaagagc gtacaggttt ttccatccgt cctgtggctg gttacttatc accaagagat 720
ttcttatcag gtttagcctt tcgagttttt cactgcactc aatatgtgag acacagttca 780
gatcccttct ataccccaga gccagatacc tgccatgaac tcttaggtca tgtcccgctt 840
ttggctgaac ctagttttgc ccaattctcc caagaaattg gcttggcttc tcttggcgct 900
tcagaggagg ctgttcaaaa actggcaacg tgctactttt tcactgtgga gtttggtcta 960
tgtaaacaag atggacagct aagagtcttt ggtgctggct tactttcttc tatcagtgaa 1020
ctcaaacatg cactttctgg acatgccaaa gtaaagccct ttgatcccaa gattacctgc 1080
aaacaggaat gtcttatcac aacttttcaa gatgtctact ttgtatctga aagttttgaa 1140
gatgcaaagg agaagatgag agaatttacc aaaacaatta agcgtccatt tggagtgaag 1200
tataatccat atacacggag tattcagatc ctgaaagaca ccaagagcat aaccagtgcc 1260
atgaatgagc tgcagcatga tctcgatgtt gtcagtgatg cccttgctaa gtcactaaat 1320
gaagatgttc ttcaagtttc tgtctttgca cttctactct tttgccatc tcttcatggg 1380
gaatgtcacc cagatacatg acttcagttc ttattttgaa tgactcctct atttgcagtt 1440
ataaccctga catctttctt gaatttttt gccccttaat tccaacgaac tcctggatgt 1500
ctatgtagat gtctcataat ttaggccaat gctgtacaac ttcatgtggc atcatccaca 1560
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aaatagatgc tagctaatct agaatcattt gaaatattga ttatctgatt tatagtttgg 2040
ttgcaaggaa atctactgta agcaaatcat aatagatagc aaatcttaga acatgtagaa 2100

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aaaaagaaat taaaaaaagc aaatcttaga acatgtagaa aaaggaaatt aaaaaataga 2160
tagcaaataa cacaaattat gcatactata tatggttatt ttcatacaac tttgataacg 2220
gtgaagaatc atacttattg aattttaaaa tgatgatgtt taaaatcact ctatgactaa 2280
agcacatgag aataaatgtt aaaggcacag ccttataatc cacaacttca gaacaatgga 2340
attttttttt tttttttttt tttttttttt tttttttttt tttgagacgg agtcttgctc 2400
tgtcgcccag gctggagtgc agtggtgcga tcttggctca ctgcaagctc cacctcccag 2460
gttcacggca ttctcctgcc tctgtctcct gagtagctgg gactacaggc gcccgccacc 2520
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tcatgcattt taaatatatg tcttcaaagc acctaggaat atgtaaatag ttacccaaat 2820
gtgagaacag aattgaacta aaagcttcgt ttataatttt tttttttttg agacagagtc 2880
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ccatgttggc caggctggtc tcgaacttct gaccgcaggt gatccatccg cctcggcctc 3060
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attcatagga agtgtttaag gtactatggt ctattttggt ctaatctttg ttttactatg 3420
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ttaaaaaaaa aaaaaaaaat aaaaa                                       3505
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<210> 322
<211> 466
<212> PRT
<213> Homo sapiens

<400> 322

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Met Ile Glu Asp Asn Lys Glu Asn Lys Asp His Ser Leu Glu Arg Gly
1               5                   10                  15
Arg Ala Ser Leu Ile Phe Ser Leu Lys Asn Glu Val Gly Gly Leu Ile
            20                  25                  30
Lys Ala Leu Lys Ile Phe Gln Glu Lys His Val Asn Leu Leu His Ile
        35                  40                  45
Glu Ser Arg Lys Ser Lys Arg Arg Asn Ser Glu Phe Glu Ile Phe Val
    50                  55                  60
Asp Cys Asp Ile Asn Arg Glu Gln Leu Asn Asp Ile Phe His Leu Leu
65                  70                  75                  80
Lys Ser His Thr Asn Val Leu Ser Val Asn Leu Pro Asp Asn Phe Thr
                85                  90                  95
Leu Lys Glu Asp Gly Met Glu Thr Val Pro Trp Phe Pro Lys Lys Ile
            100                 105                 110
Ser Asp Leu Asp His Cys Ala Asn Arg Val Leu Met Tyr Gly Ser Glu
        115                 120                 125
Leu Asp Ala Asp His Pro Gly Phe Lys Asp Asn Val Tyr Arg Lys Arg
    130                 135                 140
Arg Lys Tyr Phe Ala Asp Leu Ala Met Asn Tyr Lys His Gly Asp Pro
145                 150                 155                 160
Ile Pro Lys Val Glu Phe Thr Glu Glu Glu Ile Lys Thr Trp Gly Thr
                165                 170                 175
Val Phe Gln Glu Leu Asn Lys Leu Tyr Pro Thr His Ala Cys Arg Glu
            180                 185                 190
Tyr Leu Lys Asn Leu Pro Leu Leu Ser Lys Tyr Cys Gly Tyr Arg Glu
        195                 200                 205
Asp Asn Ile Pro Gln Leu Glu Asp Val Ser Asn Phe Leu Lys Glu Arg
```

```
    210                 215                 220
Thr Gly Phe Ser Ile Arg Pro Val Ala Gly Tyr Leu Ser Pro Arg Asp
225                 230                 235                 240
Phe Leu Ser Gly Leu Ala Phe Arg Val Phe His Cys Thr Gln Tyr Val
                245                 250                 255
Arg His Ser Ser Asp Pro Phe Tyr Thr Pro Glu Pro Asp Thr Cys His
            260                 265                 270
Glu Leu Leu Gly His Val Pro Leu Leu Ala Glu Pro Ser Phe Ala Gln
        275                 280                 285
Phe Ser Gln Glu Ile Gly Leu Ala Ser Leu Gly Ala Ser Glu Glu Ala
    290                 295                 300
Val Gln Lys Leu Ala Thr Cys Tyr Phe Phe Thr Val Glu Phe Gly Leu
305                 310                 315                 320
Cys Lys Gln Asp Gly Gln Leu Arg Val Phe Gly Ala Gly Leu Leu Ser
                325                 330                 335
Ser Ile Ser Glu Leu Lys His Ala Leu Ser Gly His Ala Lys Val Lys
            340                 345                 350
Pro Phe Asp Pro Lys Ile Thr Cys Lys Gln Glu Cys Leu Ile Thr Thr
        355                 360                 365
Phe Gln Asp Val Tyr Phe Val Ser Glu Ser Phe Glu Asp Ala Lys Glu
    370                 375                 380
Lys Met Arg Glu Phe Thr Lys Thr Ile Lys Arg Pro Phe Gly Val Lys
385                 390                 395                 400
Tyr Asn Pro Tyr Thr Arg Ser Ile Gln Ile Leu Lys Asp Thr Lys Ser
                405                 410                 415
Ile Thr Ser Ala Met Asn Glu Leu Gln His Asp Leu Asp Val Val Ser
            420                 425                 430
Asp Ala Leu Ala Lys Ser Leu Asn Glu Asp Val Leu Gln Val Ser Val
        435                 440                 445
Phe Ala Leu Leu Leu Phe Leu Pro Ser Leu His Gly Glu Cys His Pro
    450                 455                 460
Asp Thr
465
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<210> 323
<211> 1154
<212> DNA
<213> Homo sapiens

<400> 323

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cacgagggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgtcctt 60
tgtggagcct cagcagttcc ctctttcaga actcactgcc aagagccctg aacaggagcc 120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180
ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt 240
ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300
ctcatcgcag ccggcgttgt ggtctttgct cttggtttcc tgggctgcta tggtgctaag 360
actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct 420
gaggttgcag ctgctgtggt cgccttggtg tacaccacaa tggctgagca cttcctgacg 480
ttgctggtag tgcctgccat caagaaagat tatggttccc aggaagactt cactcaagtg 540
tggaacacca ccatgaaagg gctcaagtgc tgtggcttca ccaactatac ggattttgag 600
gactcaccct acttcaaaga gaacagtgcc tttcccccat tctgttgcaa tgacaacgtc 660
accaacacag ccaatgaaac ctgcaccaag caaaaggctc acgaccaaaa agtagagggt 720
tgcttcaatc agcttttgta tgacatccga actaatgcag tcaccgtggg tggtgtggca 780
gctggaattg gggcctcga gttcttttcc aactcagctc gaaggccacc tcttccagaa 840
agcctctata gcactcccat cagaagagat cacgtctttc tacaaccctc ccctccatga 900
ctttcatggc tcttagagcc tctgctgtct ctgcttcatc ctggaagtat cacaatcctc 960
caccacactg aacccctcaa ggtagggcca ggtctgatta ctttcaggtc cccagtgccc 1020
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agcacaaggc tgaggccaaa aaaaggacca ggggatggtt ataaaataaa tcaatgaatt 1080
gactgcctaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa gaaaaaaaaa 1140
aaaaaaaaaa aagt 1154

<210> 324
<211> 258
<212> PRT
<213> Homo sapiens

<400> 324
Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
1 5 10 15
Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
20 25 30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
35 40 45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
50 55 60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
65 70 75 80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
85 90 95
Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
100 105 110
Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
115 120 125
Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
130 135 140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
145 150 155 160
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
165 170 175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
180 185 190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
195 200 205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
210 215 220
Leu Glu Phe Phe Ser Asn Ser Ala Arg Arg Pro Pro Leu Pro Glu Ser
225 230 235 240
Leu Tyr Ser Thr Pro Ile Arg Arg Asp His Val Phe Leu Gln Pro Ser
245 250 255
Pro Pro

<210> 325
<211> 1076
<212> DNA
<213> Homo sapiens

<400> 325
atgcagtgct tcagcttcat taagaccatg atgatcctct tcaatttgct catctttctg 60
tgtggtgcag ccctgttggc agtgggcatc tgggtgtcaa tcgatggggc atcctttctg 120
aagatcttcg ggccactgtc gtccagtgcc atgcagtttg tcaacgtggg ctacttcctc 180
atcgcagccg gcgttgtggt ctttgctctt ggtttcctgg gctgctatgg tgctaagact 240
gagagcaagt gtgccctcgt gacgttcttc ttcatcctcc tcctcatctt cattgctgag 300
gttgcagctg ctgtggtcgc cttggtgtac accacaatgg ctgagcactt cctgacgttg 360

```
ctggtagtgc ctgccatcaa gaaagattat ggttcccagg aagacttcac tcaagtgtgg 420
aacaccacca tgaaagggct caagtgctgt ggcttcacca actatacgga ttttgaggac 480
tcaccctact tcaaagagaa cagtgccttt cccccattct gttgcaatga caacgtcacc 540
aacacagcca atgaaacctg caccgagcaa aaggctcacg accaaaaagt agagggttgc 600
ttcaatcagc ttttgtatga catccgaact aatgcagtca ccgtgggtgg tgtggcagct 660
ggaattgggg gcctcgagct ggctgccatg attgtgtcca tgtatctgta ctgcaatcta 720
caataagtcc acttctgcct ctgccactac tgctgccaca tgggaactgt gaagaggcac 780
cctggcaagc agcagtgatt gggggagggg acaggatcta acaatgtcac ttgggccaga 840
atggacctgc cctttctgct ccagacttgg ggctagatag ggaccactcc ttttaggcga 900
tgctgacttt ccttccattg gtgggtggat gggtgggggg cattccagag cctctaaggt 960
agccagttct gttgcccatt cccccagtct attaaaccct tgatatgccc cctaggccta 1020
gtggtgatcc cagtgctcta ctgggggatg agagaaaggc atttatagc ctgggc      1076
```

<210> 326
<211> 241
<212> PRT
<213> Homo sapiens

<400> 326

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Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
 1               5                  10                  15
Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
            20                  25                  30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
        35                  40                  45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
    50                  55                  60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
65                  70                  75                  80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
                85                  90                  95
Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
            100                 105                 110
Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
        115                 120                 125
Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
    130                 135                 140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
145                 150                 155                 160
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
                165                 170                 175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Glu Gln Lys Ala
            180                 185                 190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
        195                 200                 205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
    210                 215                 220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
225                 230                 235                 240
Gln
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<210> 327
<211> 2244
<212> DNA
<213> Homo sapiens

<400> 327
gggaaggaga tgcctcttcc ttcccttcaa tagtgggtta aacccagctg gcaccctctg 60
gaactacggg aacaatattc ttcaagagaa ggtcactcta ccaaagccag gagcacagta 120
ttctcaggat ctcaacaagg aagagcagac caaggttgct tctgattcct tacaaccttc 180
cgtaattcca ggcttgtggc cccaaattca gggccccacc cttccaggaa caaatcatta 240
tagtaataat ttgccttcat cttccatata ccaactaagc atgtttaact acgaacgtcc 300
aaaacacttc atccagtccc aaaacccatg tggctccaga ttgcagcctc ctggaccaga 360
aacctccagc ttctctagcc agaccaaaca gtcttccatt atcatccagc cccgccagtg 420
tacagagcaa agatttctg cctcctcaac actgagctct cacatcacca tgtcctcctc 480
tgctttccct gcttctcccc agcagcatgc tggctccaac ccaggccaaa gggttacaac 540
cacctataac cagtccccag ccagcttcct cagctccata ttaccatcac agcctgatta 600
caatagcagt aaaatccctt ccgctatgga ttccaactat caacagtcct cagctggcca 660
acctataaat gcaaagccat cccaaactgc aaatgctaag cccataccaa gaactcctga 720
tcatgaaata caaggatcaa aagaagcttt gattcaagat ttggaaagaa agctgaaatg 780
caaggacacc cttcttcata atggaaatca acgtctaaca tatgaagaga agatggctcg 840
cagattgcta ggaccacaga atgcagctgc tgtgtttcaa gctcaggatg acagtggtgc 900
acaagactcg cagcaacaca actcagaaca tgcgcgactg caagttccta catcacaagt 960
aagaagtaga tcaacctcaa ggggagatgt gaatgatcag gatgcaatcc aggagaaatt 1020
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cagaatggac ttcaaagtga gtggactgcc agctcctgat gtgtcatggt atctaaatgg 1140
aagaacagtt caatcagatg atttgcacaa aatgatagtg tctgagaagg gtcttcattc 1200
actcatcttt gaagtagtca gagcttcaga tgcaggggct tatgcatgtg ttgccaagaa 1260
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agcaccaatg tttatctaca aaccacagag caaaaaagtt ttagagggag attcagtgaa 1380
actagaatgc cagatctcgg ctatacctcc accaaagctt ttctggaaaa gaaataatga 1440
aatggtacaa ttcaacactg accgaataag cttatatcaa gataacactg gaagagttac 1500
tttactgata aaagatgtaa acaagaaaga tgctgggtgg tatactgtgt cagcagttaa 1560
tgaagctgga gtgactacat gtaacacaag attagacgtt acggcacgtc caaaccaaac 1620
tcttccagct cctaagcagt tacgggttcg accaacattc agcaaatatt tagcacttaa 1680
tgggaaaggt ttgaatgtaa aacaagcttt taacccagaa ggagaatttc agcgtttggc 1740
agctcaatct ggactctatg aaagtgaaga actttaataa ctttaccaac attggaaaac 1800
agccaactac accattagta atatatttga ttacattttt ttgaaattaa tccatagctg 1860
tattaacaga ttatggtttt aattaggtaa tatagttaat atatatttat aatattattt 1920
atcctttgac tcttgcacat tctatgtacc cctccgattt gtgaagccta caggaaatct 1980
gggtatatgg atttgtaact gcagaagact atcttaaaat acaggatttt aacatttaag 2040
tcatgcacat ttaacaatta caggttataa attagtatca actttttaaa cacatctaat 2100
gcttgtaata acgtttactg gtactgcttt ctaaatactg ttttacccgt tttctcttgt 2160
aggaatacta acatggtata gattatctga gtgttccaca gttgtatgtc aaaagaaaat 2220
aaaattcaaa tatttaaaac ggac 2244

<210> 328
<211> 498
<212> PRT
<213> Homo sapiens

<400> 328
Met Phe Asn Tyr Glu Arg Pro Lys His Phe Ile Gln Ser Gln Asn Pro
1 5 10 15
Cys Gly Ser Arg Leu Gln Pro Pro Gly Pro Glu Thr Ser Ser Phe Ser
20 25 30
Ser Gln Thr Lys Gln Ser Ser Ile Ile Ile Gln Pro Arg Gln Cys Thr
35 40 45
Glu Gln Arg Phe Ser Ala Ser Ser Thr Leu Ser Ser His Ile Thr Met
50 55 60
Ser Ser Ser Ala Phe Pro Ala Ser Pro Gln Gln His Ala Gly Ser Asn
65 70 75 80
Pro Gly Gln Arg Val Thr Thr Thr Tyr Asn Gln Ser Pro Ala Ser Phe
85 90 95

Leu Ser Ser Ile Leu Pro Ser Gln Pro Asp Tyr Asn Ser Ser Lys Ile
100 105 110

Pro Ser Ala Met Asp Ser Asn Tyr Gln Gln Ser Ser Ala Gly Gln Pro
115 120 125

Ile Asn Ala Lys Pro Ser Gln Thr Ala Asn Ala Lys Pro Ile Pro Arg
130 135 140

Thr Pro Asp His Glu Ile Gln Gly Ser Lys Glu Ala Leu Ile Gln Asp
145 150 155 160

Leu Glu Arg Lys Leu Lys Cys Lys Asp Thr Leu Leu His Asn Gly Asn
165 170 175

Gln Arg Leu Thr Tyr Glu Glu Lys Met Ala Arg Arg Leu Leu Gly Pro
180 185 190

Gln Asn Ala Ala Ala Val Phe Gln Ala Gln Asp Asp Ser Gly Ala Gln
195 200 205

Asp Ser Gln Gln His Asn Ser Glu His Ala Arg Leu Gln Val Pro Thr
210 215 220

Ser Gln Val Arg Ser Arg Ser Thr Ser Arg Gly Asp Val Asn Asp Gln
225 230 235 240

Asp Ala Ile Gln Glu Lys Phe Tyr Pro Pro Arg Phe Ile Gln Val Pro
245 250 255

Glu Asn Met Ser Ile Asp Glu Gly Arg Phe Cys Arg Met Asp Phe Lys
260 265 270

Val Ser Gly Leu Pro Ala Pro Asp Val Ser Trp Tyr Leu Asn Gly Arg
275 280 285

Thr Val Gln Ser Asp Asp Leu His Lys Met Ile Val Ser Glu Lys Gly
290 295 300

Leu His Ser Leu Ile Phe Glu Val Val Arg Ala Ser Asp Ala Gly Ala
305 310 315 320

Tyr Ala Cys Val Ala Lys Asn Arg Ala Gly Glu Ala Thr Phe Thr Val
325 330 335

Gln Leu Asp Val Leu Ala Lys Glu His Lys Arg Ala Pro Met Phe Ile
340 345 350

Tyr Lys Pro Gln Ser Lys Lys Val Leu Glu Gly Asp Ser Val Lys Leu
355 360 365

Glu Cys Gln Ile Ser Ala Ile Pro Pro Pro Lys Leu Phe Trp Lys Arg
370 375 380

Asn Asn Glu Met Val Gln Phe Asn Thr Asp Arg Ile Ser Leu Tyr Gln
385 390 395 400

Asp Asn Thr Gly Arg Val Thr Leu Leu Ile Lys Asp Val Asn Lys Lys
405 410 415

Asp Ala Gly Trp Tyr Thr Val Ser Ala Val Asn Glu Ala Gly Val Thr
420 425 430

Thr Cys Asn Thr Arg Leu Asp Val Thr Ala Arg Pro Asn Gln Thr Leu
435 440 445

Pro Ala Pro Lys Gln Leu Arg Val Arg Pro Thr Phe Ser Lys Tyr Leu
450 455 460

Ala Leu Asn Gly Lys Gly Leu Asn Val Lys Gln Ala Phe Asn Pro Glu
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Gly Glu Phe Gln Arg Leu Ala Ala Gln Ser Gly Leu Tyr Glu Ser Glu
485 490 495

Glu Leu

<210> 329
<211> 3649
<212> DNA
<213> Homo sapiens

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<210> 330
<211> 812
<212> PRT
<213> Homo sapiens

<400> 330
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Leu Asn Thr Ile Ala Glu Gly Asp Asn Val Tyr Ala Phe Gln Val Pro
35 40 45
Pro Ser Pro Ser Gln Gly Thr Leu Ser Ala His Pro Leu Gly Leu Ser
50 55 60
Ala Ser Pro Arg Leu Ala Ala Arg Glu Gly Gln Arg Phe Ser Leu Ser
65 70 75 80
Leu His Ser Glu Ser Lys Val Leu Ile Leu Phe Cys Asn Leu Val Gly
85 90 95
Ser Gly Gln Gln Ala Ser Arg Phe Gly Pro Pro Phe Leu Ile Arg Glu
100 105 110
Asp Arg Ala Val Ser Trp Ala Gln Leu Gln Gln Ser Ile Leu Ser Lys
115 120 125
Val Arg His Leu Met Lys Ser Glu Ala Pro Val Gln Asn Leu Gly Ser
130 135 140
Leu Phe Ser Ile Arg Val Val Gly Leu Ser Val Ala Cys Ser Tyr Leu
145 150 155 160
Ser Pro Lys Asp Ser Arg Pro Leu Cys His Trp Ala Val Asp Arg Val
165 170 175
Leu His Leu Arg Arg Pro Gly Gly Pro Pro His Val Lys Leu Ala Val
180 185 190
Glu Trp Asp Ser Ser Val Lys Glu Arg Leu Phe Gly Ser Leu Gln Glu
195 200 205
Glu Arg Ala Gln Asp Ala Asp Ser Val Trp Gln Gln Gln Gln Ala His
210 215 220
Gln Gln His Ser Cys Thr Leu Asp Glu Cys Phe Gln Phe Tyr Thr Lys
225 230 235 240
Glu Glu Gln Leu Ala Gln Asp Asp Ala Trp Lys Cys Pro His Cys Gln
245 250 255
Val Leu Gln Gln Gly Met Val Lys Leu Ser Leu Trp Thr Leu Pro Asp
260 265 270
Ile Leu Ile Ile His Leu Lys Arg Phe Cys Gln Val Gly Glu Arg Arg
275 280 285
Asn Lys Leu Ser Thr Leu Val Lys Phe Pro Leu Ser Gly Leu Asn Met
290 295 300
Ala Pro His Val Ala Gln Arg Ser Thr Ser Pro Glu Ala Gly Leu Gly
305 310 315 320
Pro Trp Pro Ser Trp Lys Gln Pro Asp Cys Leu Pro Thr Ser Tyr Pro
325 330 335
Leu Asp Phe Leu Tyr Asp Leu Tyr Ala Val Cys Asn His His Gly Asn
340 345 350
Leu Gln Gly Gly His Tyr Thr Ala Tyr Cys Arg Asn Ser Leu Asp Gly
355 360 365

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Gln Trp Tyr Ser Tyr Asp Asp Ser Thr Val Glu Pro Leu Arg Glu Asp
    370                 375                 380
Glu Val Asn Thr Arg Gly Ala Tyr Ile Leu Phe Tyr Gln Lys Arg Asn
385                 390                 395                     400
Ser Ile Pro Pro Trp Ser Ala Ser Ser Ser Met Arg Gly Ser Thr Ser
                405                 410                     415
Ser Ser Leu Ser Asp His Trp Leu Leu Arg Leu Gly Ser His Ala Gly
            420                 425                 430
Ser Thr Arg Gly Ser Leu Leu Ser Trp Ser Ser Ala Pro Cys Pro Ser
        435                 440                 445
Leu Pro Gln Val Pro Asp Ser Pro Ile Phe Thr Asn Ser Leu Cys Asn
    450                 455                 460
Gln Glu Lys Gly Gly Leu Glu Pro Arg Arg Leu Val Arg Gly Val Lys
465                 470                 475                     480
Gly Arg Ser Ile Ser Met Lys Ala Pro Thr Thr Ser Arg Ala Lys Gln
                485                 490                 495
Gly Pro Phe Lys Thr Met Pro Leu Arg Trp Ser Phe Gly Ser Lys Glu
            500                 505                 510
Lys Pro Pro Gly Ala Ser Val Glu Leu Val Glu Tyr Leu Glu Ser Arg
        515                 520                 525
Arg Arg Pro Arg Ser Thr Ser Gln Ser Ile Val Ser Leu Leu Thr Gly
    530                 535                 540
Thr Ala Gly Glu Asp Glu Lys Ser Ala Ser Pro Arg Ser Asn Val Ala
545                 550                 555                     560
Leu Pro Ala Asn Ser Glu Asp Gly Gly Arg Ala Ile Glu Arg Gly Pro
                565                 570                 575
Ala Gly Val Pro Cys Pro Ser Ala Gln Pro Asn His Cys Leu Ala Pro
            580                 585                 590
Gly Asn Ser Asp Gly Pro Asn Thr Ala Arg Lys Leu Lys Glu Asn Ala
        595                 600                 605
Gly Gln Asp Ile Lys Leu Pro Arg Lys Phe Asp Leu Pro Leu Thr Val
    610                 615                 620
Met Pro Ser Val Glu His Glu Lys Pro Ala Arg Pro Glu Gly Gln Lys
625                 630                 635                     640
Ala Met Asn Trp Lys Glu Ser Phe Gln Met Gly Ser Lys Ser Ser Pro
                645                 650                 655
Pro Ser Pro Tyr Met Gly Phe Ser Gly Asn Ser Lys Asp Ser Arg Arg
            660                 665                 670
Gly Thr Ser Glu Leu Asp Arg Pro Leu Gln Gly Thr Leu Thr Leu Leu
        675                 680                 685
Arg Ser Val Phe Arg Lys Lys Glu Asn Arg Arg Asn Glu Arg Ala Glu
    690                 695                 700
Val Ser Pro Gln Val Pro Pro Val Ser Leu Val Ser Gly Gly Leu Ser
705                 710                 715                     720
Pro Ala Met Asp Gly Gln Ala Pro Gly Ser Pro Pro Ala Leu Arg Ile
                725                 730                 735
Pro Glu Gly Leu Ala Arg Gly Leu Gly Ser Arg Leu Glu Arg Asp Val
            740                 745                 750
Trp Ser Ala Pro Ser Ser Leu Arg Leu Pro Arg Lys Ala Ser Arg Ala
        755                 760                 765
Pro Arg Gly Ser Ala Leu Gly Met Ser Gln Arg Thr Val Pro Gly Glu
    770                 775                 780
Gln Ala Ser Tyr Gly Thr Phe Gln Arg Val Lys Tyr His Thr Leu Ser
785                 790                 795                     800
Leu Gly Arg Lys Lys Thr Leu Pro Glu Ser Ser Phe
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<210> 331
<211> 1811
<212> DNA
<213> Homo sapiens

<400> 331
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cacagtcact actgtcgcct cagctgggaa cattggggag gatggaatcc agagctgcac 240
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cagaggccgg acagcagtgt ttgctgatca agtgatagtt ggcaatgcct ctttgcggct 420
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cacagtggtc tgggcatccc aagttgacca gggagccaac ttctcggaag tctccaatac 660
cagctttgag ctgaactctg agaatgtgac catgaaggtt gtgtctgtgc tctacaatgt 720
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gttaaccact gccttcctgg accttggagc cacggtgact gtattacatg ttgttataga 1740
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aaaaaaaaaa a 1811

<210> 332
<211> 282
<212> PRT
<213> Homo sapiens

<400> 332
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20 25 30
Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35 40 45
Gly Glu Asp Gly Ile Gln Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50 55 60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65 70 75 80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85 90 95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100 105 110

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Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
        115                 120                 125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
    130                 135                 140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn
145                 150                 155                 160
Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
                165                 170                 175
Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
            180                 185                 190
Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
        195                 200                 205
Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
    210                 215                 220
Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225                 230                 235                 240
Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
                245                 250                 255
Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
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Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys
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<210> 333
<211> 1984
<212> DNA
<213> Homo sapiens

<400> 333

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tgttttttc agccaaagcc ttgtttccat ttttgttgat gtgtactctt gctcttttag 1920
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<210> 334
<211> 258
<212> PRT
<213> Homo sapiens

<400> 334

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Lys Leu Asp Thr Ser Gly Phe Ser Ser Ile Leu Val Thr Leu Thr Lys
        35                  40                  45
Ala Ala Val Ala Leu Lys Met Gly Asp Leu Asp Met His Arg Asn Glu
    50                  55                  60
Met Lys Ser His Ser Glu Met Lys Leu Val Cys Gly Phe Ile Leu Glu
65                  70                  75                  80
Pro Arg Leu Leu Ile Gln Gln Arg Lys Gly Gln Ile Val Pro Thr Glu
                85                  90                  95
Leu Ala Leu His Leu Lys Glu Thr Gln Pro Gly Leu Leu Val Ala Ser
            100                 105                 110
Val Leu Gly Leu Gln Lys Asn Asn Lys Ile Gly Ile Glu Glu Ala Asp
        115                 120                 125
Ser Phe Phe Lys Val Leu Cys Ala Lys Asp Glu Asp Thr Ile Pro Gln
    130                 135                 140
Leu Leu Val Asp Phe Trp Glu Ala Gln Leu Val Ala Cys Leu Pro Asp
145                 150                 155                 160
Val Val Leu Gln Glu Leu Phe Phe Lys Leu Thr Ser Gln Tyr Ile Trp
                165                 170                 175
Arg Leu Ser Lys Arg Gln Pro Pro Asp Thr Thr Pro Leu Arg Thr Ser
            180                 185                 190
Glu Asp Leu Ile Asn Ala Cys Ser His Tyr Gly Leu Ile Tyr Pro Trp
        195                 200                 205
Val His Val Val Ile Ser Ser Asp Ser Leu Ala Asp Lys Asn Tyr Thr
    210                 215                 220
Glu Asp Leu Ser Lys Leu Gln Leu Pro Leu Phe Arg Ser Trp Ser His
225                 230                 235                 240
Phe Gln Lys Thr Leu Leu Pro Ala Ser Val Ser Met Phe Cys Val Val
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His Ala
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<210> 335
<211> 2180
<212> DNA
<213> Homo sapiens

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<400> 335
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agaattccta ttctgtacct ttcctctaac ttctcagatt tgtaattctt cttttgggag 1260
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tcttgtgttt gtgtcattct gtcctgagaa antgaagtca tctgaaaaat aaaatgacag 1380
aaactgaatt gtctaatgtt aactctgcac attgtaactt ttcttgttga gttagtatct 1440
taatttttac tccagcacaa gtatttaatc aaagaaaaga ttcatacatg tgaaattgga 1500
aggtatttat aaaattttta ttgctgtata ccaaactcag aattggaact ttttacattt 1560
gagtttcact ttttagaagt atgttttaag caagcaaaaa caaaatggga tgagaagaat 1620
tgaggcatgc aacccaatag cataaatgtc cttttcccc ccaaatatgg tctagatgag 1680
ttattataaa cattgttttt atttttttga gacagagttt cgctcttgtt gcccaggcta 1740
gagtgcaatg gcgccatctc ggctcaccgc aacctccacc ttcctggttc aagggatctc 1800
ctgcctcagc ctcccaagta gctgggatta caggcatgca ccaccacgcc cagctaattt 1860
ttatattctt tagtaaagac agggtttctc catgttggtc aggctggtct cgaacttctg 1920
acctcaggtg atctgcccac ctcggcctcc caaagtgctg gattacaggc gtgagcactg 1980
cacctggcct tataaatatc cttttaacta actcagtaac tgccatattt tgttgggttg 2040
tcttcttaaa agaatataag actaaagtgt taatgtcact tggtgttaca tttccttaca 2100
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aaaaaaaaaa aaaactttag 2180

<210> 336
<211> 234
<212> PRT
<213> Homo sapiens

<400> 336
Met Glu Ser Met Ala Val Ala Thr Asp Gly Gly Glu Arg Pro Gly Val
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Pro Ala Gly Ser Gly Leu Ser Ala Ser Gln Arg Arg Ala Glu Leu Arg
20 25 30
Arg Arg Lys Leu Leu Met Asn Ser Glu Gln Arg Ile Asn Arg Ile Met
35 40 45
Gly Phe His Arg Pro Gly Ser Gly Ala Glu Glu Glu Ser Gln Thr Lys
50 55 60
Ser Lys Gln Gln Asp Ser Asp Lys Leu Asn Ser Leu Ser Val Pro Ser
65 70 75 80
Val Ser Lys Arg Val Val Leu Gly Asp Ser Val Ser Thr Gly Thr Thr
85 90 95

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Asp Gln Gln Gly Gly Val Ala Glu Val Lys Gly Thr Gln Leu Gly Asp
            100                 105                 110
Lys Leu Asp Ser Phe Ile Lys Pro Pro Glu Cys Ser Ser Asp Val Asn
        115                 120                 125
Leu Glu Leu Arg Gln Arg Asn Arg Gly Asp Leu Thr Ala Asp Ser Val
    130                 135                 140
Gln Arg Gly Ser Arg His Gly Leu Glu Gln Tyr Leu Ser Arg Phe Glu
145                 150                 155                 160
Glu Ala Met Lys Leu Arg Lys Gln Leu Ile Ser Glu Lys Pro Ser Gln
                165                 170                 175
Glu Asp Gly Asn Thr Thr Glu Glu Phe Asp Ser Phe Arg Ile Phe Arg
            180                 185                 190
Leu Val Gly Cys Ala Leu Leu Ala Leu Gly Val Arg Ala Phe Val Cys
        195                 200                 205
Lys Tyr Leu Ser Ile Phe Ala Pro Phe Leu Thr Leu Gln Leu Ala Leu
    210                 215                 220
His Gly Ile Ile Gln Ile Phe Ser Gln Glu
225                 230
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<210> 337
<211> 3695
<212> DNA
<213> Homo sapiens

<400> 337

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ccgtcgcgct cgaccccgag ggcatgcggc agccgcaggg gcccccgctc ccgggctcgg 180
cggcgcgggt gaacgtgagc ggatgttcac ttcttctcca caatgaatga gtgtcactat 240
gacaagcaca tggacttttt ttataatagg agcaacactg atactgtcga tgactggaca 300
ggaacaaagc ttgtgattgt tttgtgtgtt gggacgtttt tctgcctgtt tatttttttt 360
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tacctgttgg ctaatttagc tgctgccgat ttcttcgctg gaattgccta tgtattcctg 480
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aggcacatgt caatcatgag gatgcgggtc catagcaacc tgaccaaaaa gagggtgaca 660
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gtcgtgaacc ccatcatcta ctcctacaag gacgaggaca tgtatggcac catgaagaag 1140
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tgaggtctcc attaatcact gctagatttc tttaaaaaat tttttttcat agtttaaaag 1440
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aaagtaaaaa aggtcaatgt gaaaaccctt tttgacctga aaaaggcctt agtatggtcc 1920
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tatatatata tatatatata tattcctgtt tttactgatt tttattgatt ttgttcaaag 2040
atatctgggg attggattgg ggaatgctta atctgactat tgaaagaaac atggatccct 2100
ggagtatttc agatacgggg ttaccgcccc agactgcctc ccgccagtcc acattagttc 2160
tcattttccc tcatgatggt gaaaaacagt ggagagctag taaagggttt atgcagaaaa 2220
caaggagaag agaatgtgaa gtttgaagtg cctatggaac atccagctga taatcttgcc 2280
tagtaagagc aaaagaagcc aagagaacac caacgtttaa ggagcaggta gagaaaaccc 2340
agcaaaagga cagaggaata agaggaccaa agaacaatgt taagaatcaa ggagagaggt 2400
caggcacgct ggctcatgcc tgtaatccca gcactttggg aggctgaggc aggtggatca 2460
cttgaggcca ggagtatgag accagcctgg gcaatgtggt gaaattgcat ctttactaaa 2520
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gaggcataag aatcacttga acccgggagg tggaggttgc agagtgagcc aagatcgcag 2640
cactgcactc tagtctgggt gacagagcaa gactctgtct caaaaaaaaa aaaaaaaaaa 2700
aaaaaagact agagaatgtc agggaacaca tgtgtatatt taaacaactt cactttgcat 2760
ttaaaaactc gaaggacagc gaaggtgaaa tcaattcacg ggccacctag actttccagc 2820
ctaggactag agctgtagca atgatctgtt gtgctgtaca agaaaagaga aagaggtgtt 2880
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taccaactgg tggcatgttg gatttagcat gtagaataat ttcccatctc ttatttttcc 3060
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atttagagtg tattctgatt taaaatgaga ataacttcaa ggtagatatt atagtattta 3300
tgtagtttgc aaaagaagtt tacatttttt tgctattgtg atataacatt tatgtgcaag 3360
aactacttgt aataaaagga tttgagatgt catgcttcta aatataatag cctaaaatag 3420
agaatattat gatttgaaag tgtagatttc acaaactctg tatagtatgt gggtctatct 3480
gaagctttta tcgaagctac ctataaaata aaattttaaa agatctgttc tctcttgttg 3540
aggtgcatta ttgctttgtg tattttctaa gtaaaaatat agtttgtggt aactacagca 3600
taaatttcta ttgcagaaga aaaatcaaat ttgccatgaa gtacatactc tcaatgtttt 3660
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```

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<210> 338
<211> 353
<212> PRT
<213> Homo sapiens

<400> 338
Met Asn Glu Cys His Tyr Asp Lys His Met Asp Phe Phe Tyr Asn Arg
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Ser Asn Thr Asp Thr Val Asp Asp Trp Thr Gly Thr Lys Leu Val Ile
            20                  25                  30
Val Leu Cys Val Gly Thr Phe Phe Cys Leu Phe Ile Phe Phe Ser Asn
        35                  40                  45
Ser Leu Val Ile Ala Ala Val Ile Lys Asn Arg Lys Phe His Phe Pro
    50                  55                  60
Phe Tyr Tyr Leu Leu Ala Asn Leu Ala Ala Ala Asp Phe Phe Ala Gly
65                  70                  75                  80
Ile Ala Tyr Val Phe Leu Met Phe Asn Thr Gly Pro Val Ser Lys Thr
                85                  90                  95
Leu Thr Val Asn Arg Trp Phe Leu Arg Gln Gly Leu Leu Asp Ser Ser
            100                 105                 110
Leu Thr Ala Ser Leu Thr Asn Leu Leu Val Ile Ala Val Glu Arg His
        115                 120                 125
Met Ser Ile Met Arg Met Arg Val His Ser Asn Leu Thr Lys Lys Arg
    130                 135                 140
Val Thr Leu Leu Ile Leu Leu Val Trp Ala Ile Ala Ile Phe Met Gly
145                 150                 155                 160
Ala Val Pro Thr Leu Gly Trp Asn Cys Leu Cys Asn Ile Ser Ala Cys
```

```
                165                 170                 175
Ser Ser Leu Ala Pro Ile Tyr Ser Arg Ser Tyr Leu Val Phe Trp Thr
            180                 185                 190
Val Ser Asn Leu Met Ala Phe Leu Ile Met Val Val Val Tyr Leu Arg
        195                 200                 205
Ile Tyr Val Tyr Val Lys Arg Lys Thr Asn Val Leu Ser Pro His Thr
    210                 215                 220
Ser Gly Ser Ile Ser Arg Arg Arg Thr Pro Met Lys Leu Met Lys Thr
225                 230                 235                 240
Val Met Thr Val Leu Gly Ala Phe Val Val Cys Trp Thr Pro Gly Leu
                245                 250                 255
Val Val Leu Leu Leu Asp Gly Leu Asn Cys Arg Gln Cys Gly Val Gln
            260                 265                 270
His Val Lys Arg Trp Phe Leu Leu Leu Ala Leu Leu Asn Ser Val Val
        275                 280                 285
Asn Pro Ile Ile Tyr Ser Tyr Lys Asp Glu Asp Met Tyr Gly Thr Met
    290                 295                 300
Lys Lys Met Ile Cys Cys Phe Ser Gln Glu Asn Pro Glu Arg Arg Pro
305                 310                 315                 320
Ser Arg Ile Pro Ser Thr Val Leu Ser Arg Ser Asp Thr Gly Ser Gln
                325                 330                 335
Tyr Ile Glu Asp Ser Ile Ser Gln Gly Ala Val Cys Asn Lys Ser Thr
            340                 345                 350
Ser
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<210> 339
<211> 3320
<212> DNA
<213> Homo sapiens

<400> 339
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ctgggcgggg gccgggccgg agcgggctcc agagacatgg ggtcgaccga ctccaagctg 120
aacttccgga aggcggtgat ccagctcacc accaagacgc agcccgtgga agccaccgat 180
gatgcctttt gggaccagtt ctgggcagac acagccacct cggtgcagga tgtgtttgca 240
ctggtgccgg cagcagagat ccgggccgtg cgggaagagt caccctccaa cttggccacc 300
ctgtgctaca aggccgttga gaagctggtg cagggagctg agagtggctg ccactcggag 360
aaggagaagc agatcgtcct gaactgcagc cggctgctca cccgcgtgct gccctacatc 420
tttgaggacc ccgactggag gggcttcttc tggtccacag tgcccggggc agggcgagga 480
gggcagggag aagaggatga tgagcatgcc aggcccctgg ccgagtccct gctcctggcc 540
attgctgacc tgctcttctg cccggacttc acggttcaga gccaccggag gagcactgtg 600
gactcggcag aggacgtcca ctccctggac agctgtgaat acatctggga ggctggtgtg 660
ggcttcgctc actcccccca gcctaactac atccacgata tgaaccggat ggagctgctg 720
aaactgctgc tgacatgctt ctccgaggcc atgtacctgc cccagctcc ggaaagtggc 780
agcaccaacc catgggttca gttcttttgt tccacggaga acagacatgc cctgcccctc 840
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aaccacctgc tcttctctga ctaccgggaa cccctggtgg aggaggctgc ccaggtgctc 960
attgtcactt tggaccacga cagtgccagc agtgccagcc ccactgtgga cggcaccacc 1020
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ctgtcccgca tccatcgtga ggaggacttc cagttcatcc tcaagggtat agcccggctg 1140
ctgtccaacc ccctgctcca gacctacctg cctaactcca ccaagaagat ccagttccac 1200
caggagctgc tagttctctt ctggaagctc tgcgacttca acaagaaatt cctcttcttc 1260
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ctgagcgggg agcggaactt cggggtgcgg ctgaacaaac cctactcaat ccgcgtgccc 1440
atggacatcc cagtcttcac agggacccac gccgacctgc tcattgtggt gttccacaag 1500
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atcatcacca gcgggcacca gcggttgcag cccctcttcg actgcctgct caccatcgtg 1560
gtcaacgtgt ccccctacct caagagcctg tccatggtga cygccaacaa gttgctgcac 1620
ctgctggagg ccttctccac cacctggttc ctcttctctg cygcccagaa ccaccacctg 1680
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acggacccgc ccaccattca caaggccctg cagcggcgcc ggcggacacc tgagcccttg 1860
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aagtcccagg tgtcagagga tggcaccttg cggtccctgg aacctgagcc ccagcagagc 2040
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gagaagatct gcatcgacaa gggcctgacg gatgagtctg agatcctgcg gttcctgcag 2280
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acccctcatc cttcacccaa gctctggcct ctgggtccca ccacccagcc ccccgtgtca 3240
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aaaaaaaaaa aaaaaaaaaa 3320

<210> 340
<211> 784
<212> PRT
<213> Homo sapiens

<400> 340
Met Gly Ser Thr Asp Ser Lys Leu Asn Phe Arg Lys Ala Val Ile Gln
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Leu Thr Thr Lys Thr Gln Pro Val Glu Ala Thr Asp Asp Ala Phe Trp
20 25 30
Asp Gln Phe Trp Ala Asp Thr Ala Thr Ser Val Gln Asp Val Phe Ala
35 40 45
Leu Val Pro Ala Ala Glu Ile Arg Ala Val Arg Glu Glu Ser Pro Ser
50 55 60
Asn Leu Ala Thr Leu Cys Tyr Lys Ala Val Glu Lys Leu Val Gln Gly
65 70 75 80
Ala Glu Ser Gly Cys His Ser Glu Lys Glu Lys Gln Ile Val Leu Asn
85 90 95
Cys Ser Arg Leu Leu Thr Arg Val Leu Pro Tyr Ile Phe Glu Asp Pro
100 105 110
Asp Trp Arg Gly Phe Phe Trp Ser Thr Val Pro Gly Ala Gly Arg Gly
115 120 125
Gly Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro Leu Ala Glu Ser
130 135 140
Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro Asp Thr Gln Ser
145 150 155 160

```
His Arg Arg Ser Thr Val Asp Ser Ala Glu Asp Val His Ser Leu Asp
                165                 170                 175
Ser Cys Glu Tyr Ile Trp Glu Ala Gly Val Gly Phe Ala His Ser Pro
            180                 185                 190
Gln Pro Asn Tyr Ile His Asp Met Asn Arg Met Glu Leu Leu Lys Leu
        195                 200                 205
Leu Leu Thr Cys Phe Ser Glu Ala Met Tyr Leu Pro Pro Ala Pro Glu
    210                 215                 220
Ser Gly Ser Thr Asn Pro Trp Val Gln Phe Phe Cys Ser Thr Glu Asn
225                 230                 235                 240
Arg His Ala Leu Pro Leu Phe Thr Ser Leu Leu Asn Thr Val Cys Ala
                245                 250                 255
Tyr Asp Pro Val Gly Tyr Gly Ile Pro Tyr Asn His Leu Leu Phe Ser
            260                 265                 270
Asp Tyr Arg Glu Pro Leu Val Glu Ala Gln Val Leu Ile Val Thr Leu
        275                 280                 285
Asp His Asp Ser Ala Ser Ser Ala Ser Pro Thr Val Asp Gly Thr Thr
    290                 295                 300
Thr Gly Thr Ala Met Asp Asp Ala Asp Pro Pro Gly Pro Glu Asn Leu
305                 310                 315                 320
Phe Val Asn Tyr Leu Ser Arg Ile His Arg Glu Glu Asp Phe Gln Phe
                325                 330                 335
Ile Leu Lys Gly Ile Ala Arg Leu Leu Ser Asn Pro Leu Leu Gln Thr
            340                 345                 350
Tyr Leu Pro Asn Ser Thr Lys Lys Ile Gln Phe His Gln Glu Leu Leu
        355                 360                 365
Val Leu Phe Trp Lys Leu Cys Asp Phe Asn Lys Lys Phe Leu Phe Phe
    370                 375                 380
Val Leu Lys Ser Ser Asp Val Leu Asp Ile Leu Val Pro Ile Leu Phe
385                 390                 395                 400
Phe Leu Asn Asp Ala Arg Ala Asp Gln Ser Arg Val Gly Leu Met His
                405                 410                 415
Ile Gly Val Phe Ile Leu Leu Leu Leu Ser Gly Glu Arg Asn Phe Gly
            420                 425                 430
Val Arg Leu Asn Lys Pro Tyr Ser Ile Arg Val Pro Met Asp Ile Pro
        435                 440                 445
Val Phe Thr Gly Thr His Ala Asp Leu Leu Ile Val Val Phe His Lys
    450                 455                 460
Ile Ile Thr Ser Gly His Gln Arg Leu Gln Pro Leu Phe Asp Cys Leu
465                 470                 475                 480
Leu Thr Ile Val Val Asn Val Ser Pro Tyr Leu Lys Ser Leu Ser Met
                485                 490                 495
Val Thr Ala Asn Lys Leu Leu His Leu Leu Glu Ala Phe Ser Thr Thr
            500                 505                 510
Trp Phe Leu Phe Ser Ala Ala Gln Asn His His Leu Val Phe Phe Leu
        515                 520                 525
Leu Glu Val Phe Asn Asn Ile Ile Gln Tyr Gln Phe Asp Gly Asn Ser
    530                 535                 540
Asn Leu Val Tyr Ala Ile Ile Arg Lys Arg Ser Ile Phe His Gln Leu
545                 550                 555                 560
Ala Asn Leu Pro Thr Asp Pro Pro Thr Ile His Lys Ala Leu Gln Arg
                565                 570                 575
Arg Arg Arg Thr Pro Glu Pro Leu Ser Arg Thr Gly Ser Gln Glu Gly
            580                 585                 590
Thr Ser Met Glu Gly Ser Arg Pro Ala Ala Pro Ala Glu Pro Gly Thr
        595                 600                 605
Leu Lys Thr Ser Leu Val Ala Thr Pro Gly Ile Asp Lys Leu Thr Glu
    610                 615                 620
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Lys Ser Gln Val Ser Glu Asp Gly Thr Leu Arg Ser Leu Glu Pro Glu
625                 630                 635                 640
Pro Gln Gln Ser Leu Glu Asp Gly Ser Pro Ala Lys Gly Glu Pro Ser
                645                 650                 655
Gln Ala Trp Arg Glu Gln Arg Arg Pro Ser Thr Ser Ser Ala Ser Gly
            660                 665                 670
Gln Trp Ser Pro Thr Pro Glu Trp Val Leu Ser Trp Lys Ser Lys Leu
        675                 680                 685
Pro Leu Gln Thr Ile Met Arg Leu Leu Gln Val Leu Val Pro Gln Val
    690                 695                 700
Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu Ser Glu Ile Leu
705                 710                 715                 720
Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu Pro Val Pro His
                725                 730                 735
Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly Thr Ala Met Trp
            740                 745                 750
Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg Asn Val Asp Pro
        755                 760                 765
Pro Val Trp Tyr Asp Thr Asp Val Lys Leu Phe Glu Ile Gln Arg Val
    770                 775                 780
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<210> 341
<211> 3307
<212> DNA
<213> Homo sapiens

<400> 341
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gggccggagc gggctccaga gacatggggt cgaccgactc caagctgaac ttccggaagg 120
cggtgatcca gctcaccacc aagacgcagc ccgtggaagc caccgatgat gcctttttggg 180
accagttctg ggcagacaca gccacctcgg tgcaggatgt gtttgcactg gtgccggcag 240
cagagatccg ggccgtgcgg gaagagtcac cctccaactt ggccaccctg tgctacaagg 300
ccgttgagaa gctggtgcag ggagctgaga gtggctgcca ctcggagaag gagaagcaga 360
tcgtcctgaa ctgcagccgg ctgctcaccc gcgtgctgcc ctacatcttt gaggaccccg 420
actggagggg cttcttctgg tccacagtgc ccggggcagg gcgaggaggg cagggagaag 480
aggatgatga gcatgccagg cccctggccg agtccctgct cctggccatt gctgacctgc 540
tcttctgccc ggacttcacg gttcagagcc accggaggag cactgtggac tcggcagagg 600
acgtccactc cctggacagc tgtgaataca tctgggaggc tggtgtgggc ttcgctcact 660
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catgcttctc cgaggccatg tacctgcccc cagctccgga aagtggcagc accaacccat 780
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cccaggaggg cacctccatg gagggctccc gccccgctgc ccctgcagag ccaggcaccc 1920
tcaagaccag tctggtggct actccaggca ttgacaagct gaccgagaag tcccaggtgt 1980
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cacccaagct ctggcctctg ggtcccacca cccagccccc cgtgtcagaa caatctttgc 3240
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aaaaaaa 3307

<210> 342
<211> 788
<212> PRT
<213> Homo sapiens

<400> 342
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Leu Thr Thr Lys Thr Gln Pro Val Glu Ala Thr Asp Asp Ala Phe Trp
20 25 30
Asp Gln Phe Trp Ala Asp Thr Ala Thr Ser Val Gln Asp Val Phe Ala
35 40 45
Leu Val Pro Ala Ala Glu Ile Arg Ala Val Arg Glu Glu Ser Pro Ser
50 55 60
Asn Leu Ala Thr Leu Cys Tyr Lys Ala Val Glu Lys Leu Val Gln Gly
65 70 75 80
Ala Glu Ser Gly Cys His Ser Glu Lys Glu Lys Gln Ile Val Leu Asn
85 90 95
Cys Ser Arg Leu Leu Thr Arg Val Leu Pro Tyr Ile Phe Glu Asp Pro
100 105 110
Asp Trp Arg Gly Phe Phe Trp Ser Thr Val Pro Gly Ala Gly Arg Gly
115 120 125
Gly Gln Gly Glu Glu Asp Asp Glu His Ala Arg Pro Leu Ala Glu Ser
130 135 140
Leu Leu Leu Ala Ile Ala Asp Leu Leu Phe Cys Pro Asp Phe Thr Val
145 150 155 160
Gln Ser His Arg Arg Ser Thr Val Asp Ser Ala Glu Asp Val His Ser
165 170 175
Leu Asp Ser Cys Glu Tyr Ile Trp Glu Ala Gly Val Gly Phe Ala His
180 185 190
Ser Pro Gln Pro Asn Tyr Ile His Asp Met Asn Arg Met Glu Leu Leu

```
        195                 200                 205
Lys Leu Leu Leu Thr Cys Phe Ser Glu Ala Met Tyr Leu Pro Pro Ala
    210                 215                 220
Pro Glu Ser Gly Ser Thr Asn Pro Trp Val Gln Phe Phe Cys Ser Thr
225                 230                 235                 240
Glu Asn Arg His Ala Leu Pro Leu Phe Thr Ser Leu Leu Asn Thr Val
                245                 250                 255
Cys Ala Tyr Asp Pro Val Gly Tyr Gly Ile Pro Tyr Asn His Leu Leu
            260                 265                 270
Phe Ser Asp Tyr Arg Glu Pro Leu Val Glu Glu Ala Ala Gln Val Leu
        275                 280                 285
Ile Val Thr Leu Asp His Asp Ser Ala Ser Ser Ala Ser Pro Thr Val
    290                 295                 300
Asp Gly Thr Thr Thr Gly Thr Ala Met Asp Asp Ala Asp Pro Pro Gly
305                 310                 315                 320
Pro Glu Asn Leu Phe Val Asn Tyr Leu Ser Arg Ile His Arg Glu Glu
                325                 330                 335
Asp Phe Gln Phe Ile Leu Lys Gly Ile Ala Arg Leu Leu Ser Asn Pro
            340                 345                 350
Leu Leu Gln Thr Tyr Leu Pro Asn Ser Thr Lys Lys Ile Gln Phe His
        355                 360                 365
Gln Glu Leu Leu Val Leu Phe Trp Lys Leu Cys Asp Phe Asn Lys Lys
    370                 375                 380
Phe Leu Phe Phe Val Leu Lys Ser Ser Asp Val Leu Asp Ile Leu Val
385                 390                 395                 400
Pro Ile Leu Phe Phe Leu Asn Asp Ala Arg Ala Asp Gln Ser Arg Val
                405                 410                 415
Gly Leu Met His Ile Gly Val Phe Ile Leu Leu Leu Leu Ser Gly Glu
            420                 425                 430
Arg Asn Phe Gly Val Arg Leu Asn Lys Pro Tyr Ser Ile Arg Val Pro
        435                 440                 445
Met Asp Ile Pro Val Phe Thr Gly Thr His Ala Asp Leu Leu Ile Val
    450                 455                 460
Val Phe His Lys Ile Ile Thr Ser Gly His Gln Arg Leu Gln Pro Leu
465                 470                 475                 480
Phe Asp Cys Leu Leu Thr Ile Val Val Asn Val Ser Pro Tyr Leu Lys
                485                 490                 495
Ser Leu Ser Met Val Thr Ala Asn Lys Leu Leu His Leu Leu Glu Ala
            500                 505                 510
Phe Ser Thr Thr Trp Phe Leu Phe Ser Ala Ala Gln Asn His His Leu
        515                 520                 525
Val Phe Phe Leu Leu Glu Val Phe Asn Asn Ile Ile Gln Tyr Gln Phe
    530                 535                 540
Asp Gly Asn Ser Asn Leu Val Tyr Ala Ile Ile Arg Lys Arg Ser Ile
545                 550                 555                 560
Phe His Gln Leu Ala Asn Leu Pro Thr Asp Pro Pro Thr Ile His Lys
                565                 570                 575
Ala Leu Gln Arg Arg Arg Arg Thr Pro Glu Pro Leu Ser Arg Thr Gly
            580                 585                 590
Ser Gln Glu Gly Thr Ser Met Glu Gly Ser Arg Pro Ala Ala Pro Ala
        595                 600                 605
Glu Pro Gly Thr Leu Lys Thr Ser Leu Val Ala Thr Pro Gly Ile Asp
    610                 615                 620
Lys Leu Thr Glu Lys Ser Gln Val Ser Glu Asp Gly Thr Leu Arg Ser
625                 630                 635                 640
Leu Glu Pro Glu Pro Gln Gln Ser Leu Glu Asp Gly Ser Pro Ala Lys
                645                 650                 655
Gly Glu Pro Ser Gln Ala Trp Arg Glu Gln Arg Arg Pro Ser Thr Ser
```

```
            660                 665                 670
Ser Ala Ser Gly Gln Trp Ser Pro Thr Pro Glu Trp Val Leu Ser Trp
        675                 680                 685
Lys Ser Lys Leu Pro Leu Gln Thr Ile Met Arg Leu Leu Gln Val Leu
    690                 695                 700
Val Pro Gln Val Glu Lys Ile Cys Ile Asp Lys Gly Leu Thr Asp Glu
705                 710                 715                 720
Ser Glu Ile Leu Arg Phe Leu Gln His Gly Thr Leu Val Gly Leu Leu
                725                 730                 735
Pro Val Pro His Pro Ile Leu Ile Arg Lys Tyr Gln Ala Asn Ser Gly
            740                 745                 750
Thr Ala Met Trp Phe Arg Thr Tyr Met Trp Gly Val Ile Tyr Leu Arg
        755                 760                 765
Asn Val Asp Pro Pro Val Trp Tyr Asp Thr Asp Val Lys Leu Phe Glu
    770                 775                 780
Ile Gln Arg Val
785
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<210> 343
<211> 563
<212> DNA
<213> Homo sapiens

<400> 343

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cacacgctat ggcaaatgaa gtgcaagacc tgctctcccc tcggaaaggg ggacatcctc 120
ctgcagtaaa agctggagga atgagaattt ccaaaaaaca agaaattggc accttggaaa 180
gacataccaa aaaaacagga ttcgagaaaa caagtgccat tgcaaatgtt gccaaaatac 240
agacactgga tgccctgaat gacgcactgg agaagctcaa ctataaattt ccagcaacag 300
tgcacatggc gcatcaaaaa cccacacctg ctctggaaaa ggttgttcca ctgaaaagga 360
tctacattat tcagcagcct cgaaaatgtt aagcctggat ttaaaacaca gccgtctggc 420
cagctgcctc gaatatctga cagcttagca aaaagggcca aagctttcca taggcgtgct 480
gcacttgctt ggtaaattaa gcagcttttg tatcttcccc tttgacttta ggtaataaag 540
catccaaact tgtaaaaaaa aaa                                         563
```

<210> 344
<211> 107
<212> PRT
<213> Homo sapiens

<400> 344

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Met Ala Asn Glu Val Gln Asp Leu Leu Ser Pro Arg Lys Gly Gly His
 1               5                  10                  15
Pro Pro Ala Val Lys Ala Gly Gly Met Arg Ile Ser Lys Lys Gln Glu
            20                  25                  30
Ile Gly Thr Leu Glu Arg His Thr Lys Lys Thr Gly Phe Glu Lys Thr
        35                  40                  45
Ser Ala Ile Ala Asn Val Ala Lys Ile Gln Thr Leu Asp Ala Leu Asn
    50                  55                  60
Asp Ala Leu Glu Lys Leu Asn Tyr Lys Phe Pro Ala Thr Val His Met
65                  70                  75                  80
Ala His Gln Lys Pro Thr Pro Ala Leu Glu Lys Val Val Pro Leu Lys
                85                  90                  95
Arg Ile Tyr Ile Ile Gln Gln Pro Arg Lys Cys
            100                 105
```

<210> 345
<211> 3733
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(3733)
<223> n = A,T,C or G

<400> 345
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cagacacctc atagcaacct atttatacaa agggggaaag aaacacctga gcagaatgga 180
atcattattt ttttcccaag gagaaaaccg gggtaaaggg agggaagcaa ttcaatttgg 240
agtccctgtg aatgggcttt cagaaggcaa ttaaagaaat ccactcagag aggacttggg 300
gtgaaacttg ggtcctgtgg ttttctgatt gtaagtggaa gcaggtcttg cacacgctgt 360
tggcaaatgt caggaccagg ttaagtgact ggcagaaaaa cttccaggtg gaacaagcaa 420
cccaggttct gctgcaagct tgaaggagcc tggagcggga gaaagctaac ttgaacatga 480
cctgttgcat ttggcaagtt ctagcaacat gctcctaagg aagcgataca ggcacagacc 540
atgcagactc cagttcctcc tgctgctcct gatgctggga tgcgtcctga tgatggtggc 600
gatgttgcac cctccccacc acaccctgca ccagactgtc acagcccaag ccagcaagca 660
cagccctgaa gccaggtacc gcctggactt tggggaatcc caggattggg tactggaagc 720
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aaagagggac tgggggggctg atgaggacgg ggaggtgtct gaagaagagg agttgacccc 960
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cacagccagc gtcatcctct gtttccatga tgaggcctgg tccactctcc tgcggactgt 1140
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cctcagccag caaggacaac tcaagtctgc tctcagcgaa tatgtggcca ggctggaggg 1260
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caccagagcc accggggatg tgctcgtctt catggatgcc cactgcgagt gccacccagg 1380
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agccatatct cagaangaag gaaangggna gctacagaaa nggaggttta ggattgcaga 3000
gaangatgca agnagcactt tggcccaatt ctccnagctn caacccagca gctgaaaagc 3060
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atttgggggt aag                                                    3733
```

<210> 346
<211> 639
<212> PRT
<213> Homo sapiens

<400> 346

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1               5                   10                  15
Leu Leu Leu Leu Leu Met Leu Gly Cys Val Leu Met Met Val Ala Met
            20                  25                  30
Leu His Pro Pro His His Thr Leu His Gln Thr Val Thr Ala Gln Ala
        35                  40                  45
Ser Lys His Ser Pro Glu Ala Arg Tyr Arg Leu Asp Phe Gly Glu Ser
    50                  55                  60
Gln Asp Trp Val Leu Glu Ala Glu Asp Glu Gly Glu Glu Tyr Ser Pro
65                  70                  75                  80
Leu Glu Gly Leu Pro Pro Phe Ile Ser Leu Arg Glu Asp Gln Leu Leu
                85                  90                  95
Val Ala Val Ala Leu Pro Gln Ala Arg Arg Asn Gln Ser Gln Gly Arg
            100                 105                 110
Arg Gly Gly Ser Tyr Arg Leu Ile Lys Gln Pro Arg Arg Gln Asp Lys
        115                 120                 125
Glu Ala Pro Lys Arg Asp Trp Gly Ala Asp Glu Asp Gly Glu Val Ser
    130                 135                 140
Glu Glu Glu Glu Leu Thr Pro Phe Ser Leu Asp Pro Arg Gly Leu Gln
145                 150                 155                 160
Glu Ala Leu Ser Ala Arg Ile Pro Leu Gln Arg Ala Leu Pro Glu Val
                165                 170                 175
Arg His Pro Leu Cys Leu Gln Gln His Pro Gln Asp Ser Leu Pro Thr
            180                 185                 190
Ala Ser Val Ile Leu Cys Phe His Asp Glu Ala Trp Ser Thr Leu Leu
        195                 200                 205
Arg Thr Val His Ser Ile Leu Asp Thr Val Pro Arg Ala Phe Leu Lys
    210                 215                 220
Glu Ile Ile Leu Val Asp Asp Leu Ser Gln Gln Gly Gln Leu Lys Ser
225                 230                 235                 240
Ala Leu Ser Glu Tyr Val Ala Arg Leu Glu Gly Val Lys Leu Leu Arg
                245                 250                 255
Ser Asn Lys Arg Leu Gly Ala Ile Arg Ala Arg Met Leu Gly Ala Thr
            260                 265                 270
Arg Ala Thr Gly Asp Val Leu Val Phe Met Asp Ala His Cys Glu Cys
```

```
        275                 280                 285
His Pro Gly Trp Leu Glu Pro Leu Leu Ser Arg Ile Ala Gly Asp Arg
    290                 295                 300
Ser Arg Val Val Ser Pro Val Ile Asp Val Ile Asp Trp Lys Thr Phe
305                 310                 315                 320
Gln Tyr Tyr Pro Ser Lys Asp Leu Gln Arg Gly Val Leu Asp Trp Lys
                325                 330                 335
Leu Asp Phe His Trp Glu Pro Leu Pro Glu His Val Arg Lys Ala Leu
            340                 345                 350
Gln Ser Pro Ile Ser Pro Ile Arg Ser Pro Val Val Pro Gly Glu Val
        355                 360                 365
Val Ala Met Asp Arg His Tyr Phe Gln Asn Thr Gly Ala Tyr Asp Ser
    370                 375                 380
Leu Met Ser Leu Arg Gly Gly Glu Asn Leu Glu Leu Ser Phe Lys Ala
385                 390                 395                 400
Trp Leu Cys Gly Gly Ser Val Glu Ile Leu Pro Cys Ser Arg Val Gly
                405                 410                 415
His Ile Tyr Gln Asn Gln Asp Ser His Ser Pro Leu Asp Gln Glu Ala
            420                 425                 430
Thr Leu Arg Asn Arg Val Arg Ile Ala Glu Thr Trp Leu Gly Ser Phe
        435                 440                 445
Lys Glu Thr Phe Tyr Lys His Ser Pro Glu Ala Phe Ser Leu Ser Lys
    450                 455                 460
Ala Glu Lys Pro Asp Cys Met Glu Arg Leu Gln Leu Gln Arg Arg Leu
465                 470                 475                 480
Gly Cys Arg Thr Phe His Trp Phe Leu Ala Asn Val Tyr Pro Glu Leu
                485                 490                 495
Tyr Pro Ser Glu Pro Arg Pro Ser Phe Ser Gly Lys Leu His Asn Thr
            500                 505                 510
Gly Leu Gly Leu Cys Ala Asp Cys Gln Ala Glu Gly Asp Ile Leu Gly
        515                 520                 525
Cys Pro Met Val Leu Ala Pro Cys Ser Asp Ser Arg Gln Gln Gln Tyr
    530                 535                 540
Leu Gln His Thr Ser Arg Lys Glu Ile His Phe Gly Ser Pro Gln His
545                 550                 555                 560
Leu Cys Phe Ala Val Arg Gln Glu Gln Val Ile Leu Gln Asn Cys Thr
                565                 570                 575
Glu Glu Gly Leu Ala Ile His Gln Gln His Trp Asp Phe Gln Glu Asn
            580                 585                 590
Gly Met Ile Val His Ile Leu Ser Gly Lys Cys Met Glu Ala Val Val
        595                 600                 605
Gln Glu Asn Asn Lys Asp Leu Tyr Leu Arg Pro Cys Asp Gly Lys Ala
    610                 615                 620
Arg Gln Gln Trp Arg Phe Asp Gln Ile Asn Ala Val Asp Glu Arg
625                 630                 635
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<210> 347
<211> 1891
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1891)
<223> n = A,T,C or G

<400> 347

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tattctggct ggagcaattg cactcatcat tggctttggt atttcaggga gacactccat 180
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aggcttggtc catgagttca aagaaggcaa agatgagctg tcggagcagg atgaaatgtt 360
cagaggccgg acagcagtgt ttgctgatca agtgatagtt ggcaatgcct ctttgcggct 420
gaaaaacgtg caactcacag atgctggcac ctacaaatgt tatatcatca cttctaaagg 480
caaggggaat gctaaccttg agtataaaac tggagccttc agcatgccgg aagtgaatgt 540
ggactataat gccagctcag agaccttgcg gtgtgaggct ccccgatggt tcccccagcc 600
cacagtggtc tgggcatccc aagttgacca gggagccaac ttctcggaag tctccaatac 660
cagctttgag ctgaactctg agaatgtgac catgaaggtt gtgtctgtgc tctacaatgt 720
tacgatcaac aacacatact cctgtatgat tgaaaatgac attgccaaag caacagggga 780
tatcaaagtg acagaatcgg agatcaaaag gcggagtcac ctacagctgc taaactcaaa 840
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acagggatct acagaactat ttcaccacca gatatgacct agttttatat ttctgggagg 1020
aaatgaattc atatctagaa gtctggagtg agcaaacaag agcaagaaac aaaaagaagc 1080
caaaagcaga wrkctscarw atkmcccctt agcgtggtcg cssccssagg tacaggacgt 1140
ctccccatta caactaccca atccgaagtg tcaactgtgt caggactaag aaaccctggt 1200
tttgagtaga aaagggcctg gaaagagggg agccaacaaa tctgtctgct tcctcacatt 1260
agtcattggc aaataagcat tctgtctctt tggctgctgc ctcagcacag agagccagaa 1320
ctctatcggg caccaggata acatctctca gtgaacanga gttgacaagg cctatgggaa 1380
atgcctgatg ggattatctt cagcttgttg agcttctaag tttctttccc ttcattctac 1440
cctgcaagcc aagttctgta agagaaatgc ctgagttcta gctcaggttt tcttactctg 1500
aatttagatc tccagaccct tcctggccac aattcaaatt aaggcaacaa acatatacct 1560
tccatgaang cacacacaga cttttgaaag caaggacaat gactgcttga attgaggcct 1620
tganggaatg aangcntttg aaggnaaaag aantactttn gtttccagcc cccnttnccc 1680
acactncttc atgtgttaan ccactgcnct tncctggann ccttggnang cccacggntg 1740
nactgntatt nacatngttg ttnnatagaa aanncntgat tttagannGt tnctgnatcg 1800
nttcnaagna gaatgnattw aaaatatacy attttccbaa aaaaaaaaaa aaaaaaaaaa 1860
maaagtacct cggccgcgac cacgctaagg g 1891

<210> 348
<211> 282
<212> PRT
<213> Homo sapiens

<400> 348
Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile Ile
1 5 10 15
Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly Ile Ser
20 25 30
Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala Gly Asn Ile
35 40 45
Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro Asp Ile Lys Leu
50 55 60
Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly Val Leu Gly Leu Val
65 70 75 80
His Glu Phe Lys Glu Gly Lys Asp Glu Leu Ser Glu Gln Asp Glu Met
85 90 95
Phe Arg Gly Arg Thr Ala Val Phe Ala Asp Gln Val Ile Val Gly Asn
100 105 110
Ala Ser Leu Arg Leu Lys Asn Val Gln Leu Thr Asp Ala Gly Thr Tyr
115 120 125
Lys Cys Tyr Ile Ile Thr Ser Lys Gly Lys Gly Asn Ala Asn Leu Glu
130 135 140
Tyr Lys Thr Gly Ala Phe Ser Met Pro Glu Val Asn Val Asp Tyr Asn

```
145                 150                 155                 160
Ala Ser Ser Glu Thr Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln
                165                 170                 175
Pro Thr Val Val Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser
            180                 185                 190
Glu Val Ser Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met
        195                 200                 205
Lys Val Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser
    210                 215                 220
Cys Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val
225                 230                 235                 240
Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn Ser
                245                 250                 255
Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp Ala Leu
            260                 265                 270
Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys
        275                 280
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<210> 349
<211> 1517
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1517)
<223> n = A,T,C or G

<400> 349

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gcccсttagc ccccgccccc agctgccagt ccccagcagc tcagtcctgc agtgagagtc 180
ttgggagtcc atagctaagc accaggagct gagcactgcc cgctgtgcct gcctgcaagt 240
ctgacatggc tcaggagaaa atggagctgg accttgagcc tgacacatct tatgggggaa 300
ccctgaggag atccagcagc gctcccctaa tccatgggct cagtgacctt tcacaggttt 360
tccaacctta cacacttaga actcggagga atagtacaac aattatgagc cgtcacagcc 420
tggaagaagg cctggatatg gtgaacagag aaactgcaca tgaaagggaa atgcaaacgg 480
caatgcagat aagccaatca tgggatgaga gcttgagcct gagtgacagt gattttgaca 540
agccggagaa attatattct cctaagagaa ttgacttcac tccagtttct ccagcacctt 600
cacccaccag ggattcggaa aagatgttcg tgagcagcag tggattgcca ccaagtccag 660
ttcccagtcc aagacgattt tcaagcagga gaagtcagag tccagtcaag tgcattagac 720
ccagtgttct tggtcctctt aaaagaaaag gtgaaatgga gacagaaagt cagcccaaga 780
gactcttcca aggcactacc aatatgttat ctccagatgc cgcgcaactg tctgatctca 840
gttcatgttc agatattttg gatggcagta gtagcagcag tggcttatcc tcagacccgc 900
tggctaaagg cagcgctacc gcagagtctc cagtagcatg ctccaattca tgctcttcgt 960
tcatcttgat ggatgatctc tcacccaagt gacttaacca tttctgattc aacgttttaa 1020
ctgctgtttc ctacataaaa tgtttagtgg ggaacgcaga gaactttgat ccataatgag 1080
gattaaagtt ttacagattt cacacattct gatgctatta ttactctttg gcatctctct 1140
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attttggatt tagtgattaa atctcaaatg ctgatttttg attgcttaga ggaatctttt 1260
ttcttagtgc ctcaaaaaac acctattttg agtctataca tttaagaaag gcactgatgt 1320
gtattgcctt taatgggtcc ttttccgcag caagtgatat gacagatttg atcagaaatt 1380
ctcttgcttg agagattttt ttttgtcctc tgttgactac atagtttcaa atctctcttt 1440
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tcaagaccat tatttg                                                 1517
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<210> 350

<211> 243
<212> PRT
<213> Homo sapiens

<220>
<221> VARIANT
<222> (1)...(243)
<223> Xaa = Any Amino Acid

<400> 350
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Gly Gly Thr Leu Arg Arg Ser Ser Ser Ala Pro Leu Ile His Gly Leu
20 25 30
Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg
35 40 45
Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Glu Glu Gly Leu Asp
50 55 60
Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln Thr Ala Met
65 70 75 80
Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser Asp Ser Asp
85 90 95
Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile Asp Phe Thr
100 105 110
Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly Lys Met Phe
115 120 125
Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser Pro Arg Arg
130 135 140
Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile Arg Pro Ser
145 150 155 160
Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr Glu Ser Gln
165 170 175
Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser Pro Asp Ala
180 185 190
Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu Asp Gly Ser
195 200 205
Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Xaa Xaa Gln Arg
210 215 220
Tyr Arg Arg Val Ser Ser Ser Met Leu Gln Phe Met Leu Phe Val His
225 230 235 240
Leu Asp Gly

<210> 351
<211> 248
<212> PRT
<213> Homo sapiens

<400> 351
Met Ala Gln Glu Lys Met Glu Leu Asp Leu Glu Pro Asp Thr Ser Tyr
1 5 10 15
Gly Gly Thr Leu Arg Arg Ser Ser Ser Ala Pro Leu Ile His Gly Leu
20 25 30
Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg
35 40 45
Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Glu Glu Gly Leu Asp
50 55 60

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Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln Thr Ala Met
65                  70                  75                  80
Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser Asp Ser Asp
                85                  90                  95
Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile Asp Phe Thr
            100                 105                 110
Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly Lys Met Phe
        115                 120                 125
Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser Pro Arg Arg
    130                 135                 140
Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile Arg Pro Ser
145                 150                 155                 160
Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr Glu Ser Gln
                165                 170                 175
Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser Pro Asp Ala
            180                 185                 190
Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu Asp Gly Ser
        195                 200                 205
Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Lys Gly Ser Ala
    210                 215                 220
Thr Ala Glu Ser Pro Val Ala Cys Ser Asn Ser Cys Ser Ser Phe Ile
225                 230                 235                 240
Leu Met Asp Asp Leu Ser Pro Lys
                245
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<210> 352
<211> 1529
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1529)
<223> n = A,T,C or G

<400> 352

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gccccttagc ccccgccccc agctgccagt ccccagcagc tcagtcctgc agtgagagtc 180
ttgggagtcc atagctaagc accaggagct gagcactgcc cgctgtgcct gcctgcaagt 240
ctgacatggc tcaggagaaa atggagctgg accttgagcc tgacacatct tatgggggaa 300
ccctgaggag atccagcagc gctcccctaa tccatgggct cagtgacctt tcacaggttt 360
tccaacctta cacacttaga actcggagga atagtacaac aattatgagc cgtcacagcc 420
tggtaagtat agaagaagaa ggcctggata tggtgaacag agaaactgca catgaaaggg 480
aaatgcaaac ggcaatgcag ataagccaat catgggatga gagcttgagc ctgagtgaca 540
gtgattttga caagccggag aaattatatt ctcctaagag aattgacttc actccagttt 600
ctccagcacc ttcacccacc aggggattcg gaaagatgtt cgtgagcagc agtggattgc 660
caccaagtcc agttcccagt ccaagacgat tttcaagcag gagaagtcag agtccagtca 720
agtgcattag acccagtgtt cttggtcctc ttaaaagaaa aggtgaaatg gagacagaaa 780
gtcagcccaa gagactcttc caaggcacta ccaatatgtt atctccagat gccgcgcaac 840
tgtctgatct cagttcatgt tcagatattt tggatggcag tagtagcagc agtggcttat 900
cctcagaccc gctggctaaa ggcagcgcta ccgcagagtc tccagtagca tgctccaatt 960
catgctcttc gttcatcttg atggatgatc tctcacccaa gtgacttaac catttctgat 1020
tcaacgtttt aactgctgtt tcctacataa aatgtttagt ggggaacgca gagaactttg 1080
atccataatg aggattaaag ttttacagat ttcacacatt ctgatgctat tattactctt 1140
tggcatctct cttctccaaa gttcaatttt gtgagcctag tgaccttact agtatctggt 1200
tttgctgatc tcattttgga tttagtgatt aaatctcaaa tgctgatttt tgattgctta 1260
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gaggaatctt ttttcttagt gcctcaaaaa acacctattt tgagtctata catttaagaa 1320
aggcactgat gtgtattgcc tttaatgggt ccttttccgc agcaagtgat atgacagatt 1380
tgatcagaaa ttctcttgct tgagagattt ttttttgtcc tctgttgact acatagtttc 1440
aaatctctct ttatttcatg atgatatata aattgctttt aattatatna aattttattt 1500
tctggatcag cttcaagacc attattttg                                   1529

<210> 353
<211> 252
<212> PRT
<213> Homo sapiens

<400> 353
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Gly Gly Thr Leu Arg Arg Ser Ser Ser Ala Pro Leu Ile His Gly Leu
            20                  25                  30
Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg
        35                  40                  45
Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Val Ser Ile Glu Glu
    50                  55                  60
Glu Gly Leu Asp Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met
65                  70                  75                  80
Gln Thr Ala Met Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu
                85                  90                  95
Ser Asp Ser Asp Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg
            100                 105                 110
Ile Asp Phe Thr Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe
        115                 120                 125
Gly Lys Met Phe Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro
    130                 135                 140
Ser Pro Arg Arg Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys
145                 150                 155                 160
Ile Arg Pro Ser Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu
                165                 170                 175
Thr Glu Ser Gln Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu
            180                 185                 190
Ser Pro Asp Ala Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile
        195                 200                 205
Leu Asp Gly Ser Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala
    210                 215                 220
Lys Gly Ser Ala Thr Ala Glu Ser Pro Val Ala Cys Ser Asn Ser Cys
225                 230                 235                 240
Ser Ser Phe Ile Leu Met Asp Asp Leu Ser Pro Lys
                245                 250


<210> 354
<211> 1574
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(1574)
<223> n = A,T,C or G

<400> 354
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gccccttagc ccccgccccc agctgccagt ccccagcagc tcagtcctgc agtgagagtc 180
ttgggagtcc atagctaagc accaggagct gagcactgcc cgctgtgcct gcctgcaagt 240
ctgacatggc tcaggagaaa atggagctgg accttgagcc tgacacatct tatgggggaa 300
ccctgaggag atccagcagc gctcccctaa tccatgggct cagtgacctt tcacaggttt 360
tccaacctta cacacttaga actcggagga atagtacaac aattatgagc cgtcacagcc 420
tgttgctgtc atcctcacct aatcgtattc ctagtagcag actgcatcag atcaaaaggg 480
aagaaggcct ggatatggtg aacagagaaa ctgcacatga aagggaaatg caaacggcaa 540
tgcagataag ccaatcatgg gatgagagct tgagcctgag tgacagtgat tttgacaagc 600
cggagaaatt atattctcct aagagaattg acttcactcc agtttctcca gcaccttcac 660
ccaccagggg attcggaaag atgttcgtga gcagcagtgg attgccacca agtccagttc 720
ccagtccaag acgattttca agcaggagaa gtcagagtcc agtcaagtgc attagaccca 780
gtgttcttgg tcctcttaaa agaaaaggtg aaatggagac agaaagtcag cccaagagac 840
tcttccaagg cactaccaat atgttatctc cagatgccgc gcaactgtct gatctcagtt 900
catgttcaga tattttggat ggcagtagta gcagcagtgg cttatcctca gacccgctgg 960
ctaaaggcag cgctaccgca gagtctccag tagcatgctc caattcatgc tcttcgttca 1020
tcttgatgga tgatctctca cccaagtgac ttaaccattt ctgattcaac gttttaactg 1080
ctgtttccta cataaaatgt ttagtgggga acgcagagaa ctttgatcca taatgaggat 1140
taaagtttta cagatttcac acattctgat gctattatta ctctttggca tctctcttct 1200
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ttgcctttaa tgggtccttt tccgcagcaa gtgatatgac agatttgatc agaaattctc 1440
ttgcttgaga gattttttt tgtcctctgt tgactacata gtttcaaatc tctctttatt 1500
tcatgatgat atataaattg cttttaatta tatnaaattt tatttctgg atcagcttca 1560
agaccattat tttg 1574

<210> 355
<211> 267
<212> PRT
<213> Homo sapiens

<400> 355
Met Ala Gln Glu Lys Met Glu Leu Asp Leu Glu Pro Asp Thr Ser Tyr
1 5 10 15
Gly Gly Thr Leu Arg Arg Ser Ser Ser Ala Pro Leu Ile His Gly Leu
20 25 30
Ser Asp Leu Ser Gln Val Phe Gln Pro Tyr Thr Leu Arg Thr Arg Arg
35 40 45
Asn Ser Thr Thr Ile Met Ser Arg His Ser Leu Leu Leu Ser Ser Ser
50 55 60
Pro Asn Arg Ile Pro Ser Ser Arg Leu His Gln Ile Lys Arg Glu Glu
65 70 75 80
Gly Leu Asp Met Val Asn Arg Glu Thr Ala His Glu Arg Glu Met Gln
85 90 95
Thr Ala Met Gln Ile Ser Gln Ser Trp Asp Glu Ser Leu Ser Leu Ser
100 105 110
Asp Ser Asp Phe Asp Lys Pro Glu Lys Leu Tyr Ser Pro Lys Arg Ile
115 120 125
Asp Phe Thr Pro Val Ser Pro Ala Pro Ser Pro Thr Arg Gly Phe Gly
130 135 140
Lys Met Phe Val Ser Ser Ser Gly Leu Pro Pro Ser Pro Val Pro Ser
145 150 155 160
Pro Arg Arg Phe Ser Ser Arg Arg Ser Gln Ser Pro Val Lys Cys Ile
165 170 175
Arg Pro Ser Val Leu Gly Pro Leu Lys Arg Lys Gly Glu Met Glu Thr
180 185 190
Glu Ser Gln Pro Lys Arg Leu Phe Gln Gly Thr Thr Asn Met Leu Ser

```
        195                 200                 205
Pro Asp Ala Ala Gln Leu Ser Asp Leu Ser Ser Cys Ser Asp Ile Leu
    210                 215                 220
Asp Gly Ser Ser Ser Ser Ser Gly Leu Ser Ser Asp Pro Leu Ala Lys
225                 230                 235                 240
Gly Ser Ala Thr Ala Glu Ser Pro Val Ala Cys Ser Asn Ser Cys Ser
                245                 250                 255
Ser Phe Ile Leu Met Asp Asp Leu Ser Pro Lys
            260                 265
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<210> 356
<211> 4458
<212> DNA
<213> Homo sapiens

<400> 356

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cagaccaacc ggctggcagc ccagctccgc tccgcccgcc cctgcctcgg accctgcgcc 180
tgaggaagta tcgaggcaac cctctgccac ccgaagttcg tgggtcgctc ccagagggcg 240
cgccctggag ccgagcgccc ttgggcggcc atctggaggc caggtgcggg ccgcgaaccc 300
gcgaggagcg cgcggcgggc gcggcggcga cggcaggagg aggggccggg agcccgggcg 360
ccgccgaagg acgccccgtc ctccacatgc tgccacttgg ctgagccggg cgccggcgag 420
aaggcggcgc cgctgccctg gcagctggac tgcactttgc cccgcccggg cctcagctgc 480
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gacccgcccc gggcctgagc gcaggctgcc tccgggaccc cacggctgtc cggacgtgcc 600
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cacgtgaaga gtggtgaaag ggaacattga ttactgaagt gccctggaga gggaaagcac 720
tggtcaacat cacatggaca aatttcattg ttttctaaag atggcctgga agtagtcttt 780
gccactgctt cctccacaaa cagctcttca taacatgggc tgcatgaaat caaagcaaac 840
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ggaacctcca gggaccaata ttgtgatctt ggaatatgca caccgcctgt ctcaggatat 1020
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tcttgtttgt ttgtcaagga tctctacttc ttgacacaaa tgaaccctgt ctttaataag 1620
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tatacaagaa aacaagtatg ggtacctttt acaaagagca atccaataaa tcttaaaaat 1860
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aaggcggtca ccattaaaat agaccagatg ataatgcatg aagatttaca gttgtattgc 2040
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acacacacac ctttttgttt taaaggatta agtactgttt gaagatcagt ggtaacagaa 2280
aatttgggag ggagaagaag aaattaagac atgacttgtt agaaaattaa gacttcagtt 2340
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tttaagcctg tgtatgttag atccacaata caccattggt attgaaatat aaaggttaaa 2460
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aaaaaggctt atgacctctt taatgagata aatatgtatt tgtcttgtaa gcaggcagaa 2520
aatctacctc taattttaac actaatactt tgaaacccac aatcaaatag agtgaattct 2580
ccaagttaca taagcaagga aaacattatt tgaaatatgc catgttttcg ttgcctttgg 2640
acacctcatc attcaactct aattttaccg agtcccggga tttgtactgt cccattgtac 2700
ttgcaatcta caatttatat aatagaaaaa caaccaaacc cattcataca aggatctgaa 2760
gttataaggt taagggcaga aagtttccca taagtataaa acatttccag gtcatgaaga 2820
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acaccaagac atttttgctg caaggtcatc tgctgcttaa aatgtacaat taggtatata 2940
aaataagtac aatggtgaaa acacaaagcc aggtaaagca gcatgcccca ctaaattttt 3000
cagtatacat agggacagac aagtgagttt tggttgtatc taaatatttt aatttcaggt 3060
tccttctgtg ccctgggcca ctatttccca ggggtgtgac agagatgcct gccagatcca 3120
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ttatcaccaa gcaccactcc cttgtccctg aatcacattt taatagagta caatatcttc 3240
tgtacaatat ttctgaaaca cttatgtctg aaatatatgc tgtattgtat gttaacccat 3300
gacatatatg aactacaagg cttgcataat cagtgagcta gtggataaat caagacagga 3360
gcaaatggga gaaagatgaa taaacaaatg aaaaaagatg aataaatgaa taagagagat 3420
gaataaacaa atttacatta catgtgatag ttatcatggt atggccttca tgacaagatg 3480
gatgagaata tcactgatag gatattagcc ttctttcata tctttatatt gaaatatggg 3540
ctttacttca atttgaaggt ctttcatgaa caataaaaga gagtagaagg actgtctgag 3600
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<210> 357
<211> 127
<212> PRT
<213> Homo sapiens

<400> 357

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            20                  25                  30
Gly Pro Asp Gln Pro Ala Gly Ser Pro Ala Pro Leu Arg Pro Pro Leu
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Pro Arg Thr Leu Arg Leu Arg Lys Tyr Arg Gly Asn Pro Leu Pro Pro
    50                  55                  60
Glu Val Arg Gly Ser Leu Pro Glu Gly Ala Pro Trp Ser Arg Ala Pro
65                  70                  75                  80
Leu Gly Gly His Leu Glu Ala Arg Cys Gly Pro Arg Thr Arg Glu Glu
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<211> 1168
<212> DNA
<213> Homo sapiens

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<210> 359
<211> 4458
<212> DNA
<213> Homo sapiens

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<210> 360
<211> 583
<212> DNA
<213> Homo sapiens

<400> 360

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<210> 361
<211> 125
<212> PRT
<213> Homo sapiens

<400> 361
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Thr Gly Val Cys Pro Glu Leu Gln Ala Asp Gln Asn Cys Thr Gln Glu
35 40 45
Cys Val Ser Asp Ser Glu Cys Ala Asp Asn Leu Lys Cys Cys Ser Ala
50 55 60
Gly Cys Ala Thr Phe Cys Leu Leu Cys Pro Asn Asp Lys Glu Gly Ser
65 70 75 80
Cys Pro Gln Val Asn Ile Asn Phe Pro Gln Leu Gly Leu Cys Arg Asp
85 90 95
Gln Cys Gln Val Asp Thr Gln Cys Pro Gly Gln Met Lys Cys Cys Arg
100 105 110
Asn Gly Cys Gly Lys Val Ser Cys Val Thr Pro Asn Phe
115 120 125

<210> 362
<211> 3310
<212> DNA
<213> Homo sapiens

<400> 362
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<210> 363
<211> 732
<212> PRT
<213> Homo sapiens

<400> 363

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Gln Ala Lys Lys Val Ile Thr Met Phe Val Gln Arg Gln Val Phe Ala
        35                  40                  45
Glu Asn Lys Asp Glu Ile Ala Leu Val Leu Phe Gly Thr Asp Gly Thr
    50                  55                  60
Asp Asn Pro Leu Ser Gly Gly Asp Gln Tyr Gln Asn Ile Thr Val His
65                  70                  75                  80
Arg His Leu Met Leu Pro Asp Phe Asp Leu Leu Glu Asp Ile Glu Ser
                85                  90                  95
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Lys Ile Gln Pro Gly Ser Gln Gln Ala Asp Phe Leu Asp Ala Leu Ile
            100                 105                 110
Val Ser Met Asp Val Ile Gln His Glu Thr Ile Gly Lys Lys Phe Glu
        115                 120                 125
Lys Arg His Ile Glu Ile Phe Thr Asp Leu Ser Ser Arg Phe Ser Lys
    130                 135                 140
Ser Gln Leu Asp Ile Ile Ile His Ser Leu Lys Lys Cys Asp Ile Ser
145                 150                 155                 160
Leu Gln Phe Phe Leu Pro Phe Ser Leu Gly Lys Glu Asp Gly Ser Gly
                165                 170                 175
Asp Arg Gly Asp Gly Pro Phe Arg Leu Gly Gly His Gly Pro Ser Phe
            180                 185                 190
Pro Leu Lys Gly Ile Thr Glu Gln Gln Lys Glu Gly Leu Glu Ile Val
        195                 200                 205
Lys Met Val Met Ile Ser Leu Glu Gly Glu Asp Gly Leu Asp Glu Ile
    210                 215                 220
Tyr Ser Phe Ser Glu Ser Leu Arg Lys Leu Cys Val Phe Lys Lys Ile
225                 230                 235                 240
Glu Arg His Ser Ile His Trp Pro Cys Arg Leu Thr Ile Gly Ser Asn
                245                 250                 255
Leu Ser Ile Arg Ile Ala Ala Tyr Lys Ser Ile Leu Gln Glu Arg Val
            260                 265                 270
Lys Lys Thr Trp Thr Val Val Asp Ala Lys Thr Leu Lys Lys Glu Asp
        275                 280                 285
Ile Gln Lys Glu Thr Val Tyr Cys Leu Asn Asp Asp Asp Glu Thr Glu
    290                 295                 300
Val Leu Lys Glu Asp Ile Ile Gln Gly Phe Arg Tyr Gly Ser Asp Ile
305                 310                 315                 320
Val Pro Phe Ser Lys Val Asp Glu Glu Gln Met Lys Tyr Lys Ser Glu
                325                 330                 335
Gly Lys Cys Phe Ser Val Leu Gly Phe Cys Lys Ser Ser Gln Val Gln
            340                 345                 350
Arg Arg Phe Phe Met Gly Asn Gln Val Leu Lys Val Phe Ala Ala Arg
        355                 360                 365
Asp Asp Glu Ala Ala Ala Val Ala Leu Ser Ser Leu Ile His Ala Leu
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Asp Asp Leu Asp Met Val Ala Ile Val Arg Tyr Ala Tyr Asp Lys Arg
385                 390                 395                 400
Ala Asn Pro Gln Val Gly Val Ala Phe Pro His Ile Lys His Asn Tyr
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Glu Cys Leu Val Tyr Val Gln Leu Pro Phe Met Glu Asp Leu Arg Gln
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Tyr Met Phe Ser Ser Leu Lys Asn Ser Lys Lys Tyr Ala Pro Thr Glu
        435                 440                 445
Ala Gln Leu Asn Ala Val Asp Ala Leu Ile Asp Ser Met Ser Leu Ala
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Lys Lys Asp Glu Lys Thr Asp Thr Leu Glu Asp Leu Phe Pro Thr Thr
465                 470                 475                 480
Lys Ile Pro Asn Pro Arg Phe Gln Arg Leu Phe Gln Cys Leu Leu His
                485                 490                 495
Arg Ala Leu His Pro Arg Glu Pro Leu Pro Pro Ile Gln Gln His Ile
            500                 505                 510
Trp Asn Met Leu Asn Pro Pro Ala Glu Val Thr Thr Lys Ser Gln Ile
        515                 520                 525
Pro Leu Ser Lys Ile Lys Thr Leu Phe Pro Leu Ile Glu Ala Lys Lys
    530                 535                 540
Lys Asp Gln Val Thr Ala Gln Glu Ile Phe Gln Asp Asn His Glu Asp
545                 550                 555                 560
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Gly Pro Thr Ala Lys Lys Leu Lys Thr Glu Gln Gly Gly Ala His Phe
                565                 570                 575
Ser Val Ser Ser Leu Ala Glu Gly Ser Val Thr Ser Val Gly Ser Val
            580                 585                 590
Asn Pro Ala Glu Asn Phe Arg Val Leu Val Lys Gln Lys Lys Ala Ser
        595                 600                 605
Phe Glu Glu Ala Ser Asn Gln Leu Ile Asn His Ile Glu Gln Phe Leu
    610                 615                 620
Asp Thr Asn Glu Thr Pro Tyr Phe Met Lys Ser Ile Asp Cys Ile Arg
625                 630                 635                 640
Ala Phe Arg Glu Glu Ala Ile Lys Phe Ser Glu Glu Gln Arg Phe Asn
                645                 650                 655
Asn Phe Leu Lys Ala Leu Gln Glu Lys Val Glu Ile Lys Gln Leu Asn
            660                 665                 670
His Phe Trp Glu Ile Val Val Gln Asp Gly Ile Thr Leu Ile Thr Lys
        675                 680                 685
Glu Glu Ala Ser Gly Ser Ser Val Thr Ala Glu Glu Ala Lys Lys Phe
    690                 695                 700
Leu Ala Pro Lys Asp Lys Pro Ser Gly Asp Thr Ala Ala Val Phe Glu
705                 710                 715                 720
Glu Gly Gly Asp Val Asp Asp Leu Leu Asp Met Ile
                725                 730
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